A RETRO-PROSPECTIVE STUDY OF PHYSIOLOGICAL PACING AND ITS SHORT TERM OUTCOMES

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I hereby declare that the thesis entitled **"A RETRO-PROSPECTIVE STUDY OF PHYSIOLOGICAL PACING AND ITS SHORT TERM OUTCOMES"** submitted towards partial fulfillment of the requirements for the award of **DM CARDIOLOGY** degree to BFUHS is a compilation of original work carried out by me under the supervision of **Dr. Naved Aslam,** Professor, Department of Cardiology, **Dr. Shibba Takkar Chhabra**, Professor, Department of Cardiology, & **Dr. Abhishek Goyal**, Professor, Department of Cardiology. No part of this thesis has formed the basis for the award of any degree previously.

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Dedicated

to

my family, friends

&

Teachers

LIST OF ABBREVIATIONS

AF	-	Atrial Fibrillation
AVN	-	Atrio-ventricular Node
CAD	-	Coronary artery disease
CRT	-	Cardiac resynchronization therapy
CSP	-	Conduction system pacing
DCMP	-	Dilated cardiomyopathy
DM	-	Diabetes mellitus
ECG	-	Electrocardiography
EGM	-	Electro gram
HB	-	His Bundle
HBP	-	His Bundle Pacing
HTN	-	Hypertension
ICMP	-	Ischemic cardiomyopathy
LBB	-	Left Bundle Branch
LBBAP	-	Left Bundle Branch Area Pacing
LBBB	-	Left Bundle Branch Block
LVAT	-	Left ventricular activation time
LVEF	-	Left ventricular ejection fraction
NYHA	-	New York Heart Association
PICM	-	Pacemaker induced cardiomyopathy
QRSd	-	QRS duration
SSS	-	Sick sinus syndrome

ABSTRACT

Introduction- Physiological pacing is a recent technique to capture the conduction system. It has been suggested as an effective alternative to conventional RV pacing with wide acceptance however is limited by scarcity of data and outcomes.

Aim- To study success rate, pacing parameters, echocardiographic features and clinical status of physiological pacing and its short term outcomes.

Material And Methods- We conducted an ambispective analytical study involving patients requiring pacing for various indications for duration of 1 year, with a 6-month follow-up who underwent CSP. The study aimed to assess the success rate of CSP and evaluate clinical and electrophysiological parameters at baseline and at 6 months of follow-up.

Result- A total of 42 non-consecutive patients were included with mean age of 62.76 ± 8.34 years. Successful physiological pacing was achieved in 95% with significant decrease in mean QRSd [(133.14 ± 13.48) vs. (111.83 ± 14.53);p=0.001]. Follow up showed stable lead parameters at 6 months, Capture threshold 0.66±0.18 V vs. 0.67 ± 0.17 V, p=0.032, QRS duration 111.83 ± 14.53 msecs vs.115.24 ± 10.86 msecs,p=0.003) with improvement of NYHA status and LVEF% of 46.70±11.14% vs 48.17%±9.53%; p=0.002.

Conclusion- Physiological pacing ensures stable lead parameters at low pacing thresholds with narrower QRS duration at high success rates.

Keywords: His- bundle pacing, Left bundle branch pacing, Cardiac-Electrophysiology, Brady-arrhythmias, Physiological pacing.

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KEY TO MASTER CHART

GENDER

1 - MALE

2 - FEMALE

SYMPTOMS

1 - SYNCOPE

2 - PRE-SYNCOPE

3 - BREATHLESSNESS

CO-MORBIDITIES

1 - HYPERTENSION

2 - CORONARY ARTERY DISEASE

3 - HYPOTHYROIDISM

4 - DIABETES MELLITUS

5 - VALVULAR HEART DISEASE

6 - DILATED CARDIOMYOPATHY

BASELINE RHYTHM

1 - SICK SINUS SYNDROME

2 - ATRIO-VENTRICULAR NODE

QRS MORPHOLOGY

1 - NORMAL

2 - LBBB

3 - LPFB

4 - LAFB

5 - RBBB

LBB POTENTIAL

0 - NO

1 - YES

CAPTURE

1 - SELECTIVE

2 - NON-SELECTIVE

3 - LEFT POSTERIOR FASCICULAR

4 - MYOCARDIAL

COMPLICATIONS

0 - NO

1 - YES

MR/AR/TR/PR

0 - NONE

1 - MILD

2 - MODERATE

3 - SEVERE

INTRODUCTION

Cardiac Conduction system disease constitutes as a major portion of cardiovascular related diseases with an increasing incidences due to ageing of general population in the era of modern medicine. A recent post hoc analysis of a randomized clinical trial amongst 6004 patients randomized to a control group and ILR (implantable loop recorder) group to detect screening of AF and any bradyarrythmias concluded a 6-fold increase in bradyarrhythmia diagnoses and a significant increase in pacemaker implantations.[1] Data on prevalence of bradyarrythmia has been lacking and few studies have reported up to 2-5% with increasing incidence with Age, History of Hypertension, coronary artery disease and congenital heart diseases.[1] Till date, cardiac pacing has been the gold standard treatment of choice for any symptomatic bradyarrythmias due to sinus node dysfunction or Atrio-ventricular nodal diseases since the invention of cardiac pacing in the 1950s.Conventional pacing has so far been beneficial in restoring of the rhythm; however has modest risks for development of cardiomyopathy, heart failure and AF.[2] These risks now can potentially be overcome by revolutionary technique of physiological pacing or Conduction system pacing (CSP). This innovative procedure involves capture of a part of naturally existing conduction pathway like His Bundle or Left bundle branch which leads to a synchronous activation of ventricles at low thresholds which further also prevents battery depletion.

Earlier works for search of an ideal pacing site has been shown to be difficult with a low success rate and somewhat experimental with case to case variability and done with use of conventional or modified leads.[3-5] Recent advances have explored the benefits of Physiological pacing with further substantial advancement in development of dedicated sheath delivery system, pacing leads, EP recording system and electrodes. The data on this ideal technique is still insufficient and still relatively new with lack of short and long term data.

Conduction system of heart is a complex anatomical structure involving SA node, Internodal tracts, AV node, His Bundle, Bundle branches, Purkinje fibers. These are specialized connective tissue with each having different electrophysiological properties. The bundle (HB) is characterized by its unique longitudinal division, which is due to the intricate partitioning of its elongated and oblong cells by collagen fibers. Unlike the atrioventricular (AV) node, the fibers within the HB are arranged in strands that are predetermined for the left or right bundle branches.[6] Bundle branch block (BBB) can be caused by conduction delays within the HB, and placing the pacing lead distal to the site of BBB can reverse it. It is important to note that what are traditionally considered "infrahisian" blocks are actually "intrahisian" blocks. This was first described by **Narula et al** [5] as theory of longitudinal dissociation in the His Bundle which also demonstrated that the electrotonic potential remains largely in a direction parallel to the running of the cells within the bundle; while almost zero in a direction perpendicular to it. Similarly Output dependence is characterized by the recruitment of distal fibers closely bordering the abnormal myocardium, which is stimulus-dependent. Increasing stimulus strength can cause a functional block that mimics the native conduction through the His Purkinje system. Patients with His Purkinje disease may have relatively proximal disease, and pacing distal to the site of block can overcome the block, resulting in a narrow QRS.[7] However, virtual electrode polarization, which was initially studied in the setting of defibrillation, remains an alternative theory to explain HBP-mediated QRS narrowing.[8]

Whether or not this QRS narrowing can overcome the detrimental effects of conventional RV pacing in long term is still under research, however results of few short term outcomes have been promising. Various studies evaluating the synchronous activation achieved by physiological pacing have shown to be superior to RV conventional pacing. Along with the

synchronous activation this technique has proven to be beneficial in terms of pacing parameters like stable and low pacing thresholds, larger R wave amplitude. Along with Pacemaker indications, the technique of physiological pacing has now also been proven to be beneficial as an alternative to cardiac resynchronization therapy in patients with heart failure with reduced ejection fraction and LBBB. Recommendations for physiological pacing have been limited in guidelines as they still lack substantial data and long term outcomes.[9]

Physiological pacing is now well established new emerging technique and rapidly accepted which still lacks substantial data and needs more evidences and experiences from different centers to support its potential benefits. Few Studies also lack echocardiographic features and follow-ups. We hereby conducted a retro-prospective study with an aim to study and compare on follow up of clinical, echocardiographic, ECG and lead parameters of physiological pacing which will increase the knowledge of this novel technique and add to existing data.

AIM AND OBJECTIVES

1. To study safety, success rate, complications and effects of physiological pacing and its short-term clinical outcomes on 6 months of follow up.
2. To study and compare Electrocardiogram and Transthoracic Echocardiographic parameters of Physiological pacing post pacemaker implantation and on 6 months of follow up.
3. To study and compare lead parameters of Physiological pacing, post-pacemaker implantation and on 6 months of follow up.

REVIEW OF LITERATURE

Conduction system pacing or Physiological pacing is specialized technique that involves placement of permanent pacing lead along different sites of cardiac conduction system with an aim to overcome atrio-ventricular (AV) conduction disease and delay, thereby providing in more synchronized and physiological type of biventricular activation.[10] The advances of physiological pacing involve (a) His bundle and (b) Left bundle branch area pacing. These innovative techniques of capture of normal cardiac conduction tissue using selective delivery sheaths and pacing leads has helped achieve a more synchronous ventricular rhythm than conventional Right ventricular apical pacing due to activation and transmission of pacing impulse through normal cardiac conduction system. Recent studies have shown physiological pacing to be **highly successful, safe, and feasible with low pacing thresholds, narrower QRS durations with stable pacing parameters.** [11-13]

1. Anatomical consideration

Cardiac conduction system consists of specialized tissues with unique electrophysiological properties. The elucidation of electrical connection from atrioventricular node (AVN) through the cardiac skeleton into the ventricular portion of the conduction system, known as Bundle of His, is attributed to **Wilhelm His Jr** in 1893.[14] However work done by **Tawara et al**[15] in 1908, later verified the existence of His-bundle along with clear identification of specialized conduction tissues that span from atrial septum to ventricular apex, including right and left bundle branches and purkinje fibers. His bundle is a chord like structure of about 20mm in length and 4mm in diameter, originating as antero-superior extension from the compact AV node. It further penetrated into fibrous body of septum and emerges out after getting encased in a fibrous sheath. It further passes along the postero-inferior margin of membranous inter-ventricular septum.[16]

Anatomically His Bundle has got 3 variants[16]

a. Type I (47%) – covered by a thin layer of myocardial fibers.
b. Type II (32%) – covered by a thick layer of myocardial fibers.
c. Type III (21%) – naked with no insulation from surrounding myocardial fibers.

The fibers within the His bundle are arranged parallel and pre destined to be Left Posterior fascicle, Left Anterior fascicle and Right Bundle branch. At the crest of muscular inter-ventricular septum, Bundle of His (HB) continues as the right bundle branch (Figure 2). The left bundle (LB) fans out as it descends in the subendocardium of the septal surface of the left ventricle into three interconnecting fascicles after the proximal 2 cm.[17]

2. Need for Physiological pacing

Since first pacemaker implanted in 1958 by Åke Senning,[18] approach to permanent cardiac pacing has been similar with use of Trans venous pacing lead placed at right ventricular apex with proven benefits of restoring rhythm. It has been the mainstay treatment of choice for symptomatic bradyarrythmias for many years. However, the detrimental effects of Right ventricular apical pacing (RVAP) have been very well established due to electrical and mechanical dyssynchrony. The abnormal ventricular activation and contraction, due to this electrical and mechanical dyssynchrony by conventional RVA pacing results in adverse left ventricular (LV) remodeling and predispose some patients to recurrent heart failure hospitalizations, atrial arrhythmias, and increased mortality. This has recently been termed as Pacing-induced cardiomyopathy (PIC) which varies, but the most accepted definition combines both echocardiographic and clinical features, including an LVEF of <50%, an absolute decline in LVEF by ≥10%, and/or new-onset HF symptoms or AF after pacemaker implantation.[19] The prevalence of PIC ranges from 6% to 25%, with an overall pooled prevalence of 12%. While most patients

undergoing RV pacing do not develop PIC, several factors are associated with an increased risk, such as male sex, chronic kidney disease, previous myocardial infarction, pre-existing AF, baseline LVEF, native QRS duration, RV pacing burden, and paced QRS duration.[19]

These findings were based from results of **MOST**[20] (Mode Selection Trial), a multicenter, double-blind, randomized, controlled trial including 2,010 patients with two groups receiving a Dual-chamber pacing (n=1,014) and a Single-chamber ventricular pacing (n=996) showed new onset AF in 21.4% vs. 27.1% patients (HR 0.77; 95% CI 0.64-0.92; P=0.004) and Hospitalization for heart failure in 10.3% vs. 12.3% (HR 0.73; 95% CI 0.56-0.95; P=0.02) at median follow- up of 3 years. Further published results from this trial at 6 year follow-up showed that Cumulative percent ventricular paced (Cum%VP) which was greater in DDDR versus VVIR (90% versus 58%, *P*=0.001) is a more stronger predictor of HF hospitalization with Cum%VP of more than 40% [hazard ratio HR, 2.99 (95% CI, 1.15 to 7.75)] and Risk of AF increased linearly with Cum%VP from 0% to 85% in both groups (DDDR, HR 1.36 [95% CI, 1.09, 1.69]; VVIR, HR 1.21 [95% CI 1.02, 1.43], for each increase of 25% in Cum%VP. Similarly, **DAVID trial**[21] (Dual-chamber pacing or ventricular backup pacing in patients with an implantable defibrillator) and **CTOPP**[22] (Canadian Trial of Physiological Pacing) trial also showed increased risk of development of Atrial fibrillation and Hospitalization for heart failures. Improvements with DDD pacing on comparison of Single-chamber ventricular pacing in other studies have been modest at best; hence a need for a more targeted physiological approach for cardiac pacing is obligated. Other ventricular pacing sites, such as the right ventricular septal (RVS) and right ventricular outflow tract (RVOT), have also been developed to minimize these adverse effects; however their long term outcomes have not been demonstrated to be superior to RVAP. A meta-analysis of 12 studies comprising 2670 patients (1655 with an apical and 1015 with a non-apical RV lead position) showed LVESV reduction and

functional status improvement were similar in patients with Right ventricular apical and non-apical pacing (SMD 0.13, 95% CI: -0.24 to 0.50, P = 0.48; OR 1.08, 95% CI: 0.81 to 1.45, P = 0.60, respectively). Hence the need for a better and more physiological pacing was persuaded in hope to provide better outcomes.[23-24]

3. Early works on physiological pacing

Early works to show feasibility of his bundle pacing includes work of **Narula et al (1970)**,[5] who used a multipolar catheter to record His bundle signals just above septal leaflet of tricuspid valve at the membranous septum. **Desmukh et al (2000)**[25] used a conventional fixed screw with non-retractable helix of 1.5mm and successfully performed permanent Distal His bundle pacing in a total of 12 out of 18 patients (66.67%) of Chronic AF, DCMP and QRSd (≤120 msecs)**.** Another observation noted during the study was significant lower pacing thre-sholds were achieved on slight advancement of pacing lead concluding that 1.5 mm helix was inadequate to sufficiently penetrate the membranous septum which led to advancements and development of dedicated sheaths and leads in recent times.

Catanzariti et al.[26] conducted a study that showed significant improvements in left ventricular (LV) dyssynchrony, reduced mitral regurgitation (MR), and increased LV ejection fraction (LVEF) in patients undergoing Hisian or Para-Hisian pacing compared to acute right ventricular apical pacing. Other subsequent studies, such as **Zanon et al.** [27] which demonstrated improved coronary perfusion with HBP when compared to RV apical pacing, and **Occhetta et al.**[28] which reported additional benefits of improved New York Heart Association (NYHA) class, exercise tolerance, and quality of life scores in patients who underwent non-selective HBP compared to RV apical pacing.

A randomized study **by Kronborg MB et al** (2011),[29] of patients with high-grade atrioventricular block and narrow complex QRS and LVEF>0.40, HBP was achieved in over 80% of patients. In this study, patients also had RV septal lead but were randomized to either RV septal pacing or HBP with crossover to the other mode after 12 months showed HBP preserved LVEF and mechanical synchrony as compared with RV septal pacing.

In a large patient series of atrioventricular block (N=100), by **Vijayaraman P et al** (2015)[30] showed a similar success rates (84%), and better success rates were noted when the underlying etiology was atrioventricular nodal block compared to infranodal block. Additionally, a large observational cohort study showed that HBP reduced the combined end point of all-cause mortality, heart failure hospitalization, and upgrade to biventricular pacing when compared to RV pacing, with a trend towards reduced mortality in the HBP group (17.2% versus 21.4%; P=0.06). Investigators suggested that several factors could have contributed to this trend, such as the elimination of ventricular dyssynchrony, reduction in HF, reduction in dispersion of ventricular repolarization, QRS narrowing, and reduction in T peak to T end.

Multiple studies have demonstrated the feasibility and benefits of HBP over RV pacing in patients with atrial fibrillation post-atrioventricular nodal ablation.[31-34] In 2013, HBP was also tested as an alternative pacing modality in patients requiring cardiac resynchronization therapy (CRT) but failing LV implantation, with a success rate of 9 out of 16 patients, mostly using nonselective HBP. This resulted in improvements in NYHA functional class, LVEF, and LV systolic and diastolic dimensions.[35] Subsequent small crossover comparison studies and randomized single center cohort studies to assess the feasibility and effectiveness of HBP in patients with CRT indication also showed comparable benefits of HBP and

CS-LV lead in improving NYHA functional class, quality of life, 6-minute walk distance, and LVEF.[36-39]

4. His Bundle Pacing Technique

Deshmukh et al. (2000)[25] used standard pacing leads by reshaping the stylet for lead placement by targeting the site with largest His deflection recorded from the electrophysiology mapping catheter. This technique was abandoned due to high pacing thresholds and frequent lead dislodgements. Since then specialized sheaths (C304, C315His and C304His, Selectsite; Medtronic) and pacing leads (3830 Selectsecure; Medtronic) developed for physiological pacing has made the technique more feasible with higher success implant rates as depicted in Figure 4.

HBP is performed by using continuous recording of intracardiac electrograms and 12-lead ECG in an electrophysiology (EP) recording system. After obtaining venous access, the C315 HIS sheath is introduced over the guidewire and placed across the tricuspid valve. The sheath has a proximal curve to point towards the tricuspid annulus and a septal curve to direct the lead towards the His region (as depicted in Figure 4). A 3830 Selectsecure lead is then advanced just exposing the helix outside the sheath. His Bundle signals are recorded directly from the pacing lead tip in a unipolar connection, and are simultaneously recorded in the EP system. Both the atrial and ventricular parts of the membranous septum can be targeted for HBP. If a predominant atrial signal is recorded, the sheath is moved gently forward with clockwise rotation aiming for a larger His signal with a small or no atrial component. Once an atrial to ventricular electrogram ratio of 1:2 or greater is noted, the sheath is pointed toward the superior-anterior septum or midseptum by minimal clockwise or counter-clockwise rotation, respectively. Once a near-field His electrogram is identified, pacing is performed at 5 V at 1 ms to assess His capture. Following identification of the His location, the fluoroscopic image is saved as a reference. The sheath is held steady, and the pacing lead is slowly

rotated clockwise approximately 5 times without releasing the lead between rotations. This allows the torque to be transmitted along the length of the lead to the lead tip. If the lead is anchored well, it will rotate back counterclockwise to release the excess torque. Once the lead is fixed, the sheath is with- drawn to the high right atrium until an adequate loop (slack) is formed. Sensing and pacing thresholds are then checked in both unipolar and bipolar configurations. HBP threshold is preferably tested at a pulse width of 1 ms to allow for a lower capture voltage. In most patients, a His bundle capture threshold of 2.0 V at 1 ms is acceptable.

In a study by **Gu et al.** [40] it was demonstrated that performing contrast angiography prior to lead implantation for visualization of the tricuspid valve annulus resulted in a shorter fluoroscopic time (7.1 versus 10.1 minutes) with comparable capture thresholds, although procedural success rates were not significantly different. Another study by **Zanon et al.** (4) showed that His bundle pacing (HBP) could be performed primarily using an electro gram with minimal or no fluoroscopy and achieved high success rates. In this study, the pacing lead was advanced through a standard 7 Fr introducer and unipolar threshold measurement was performed before fixing the lead in the membranous septum. HBP could be safely performed in 95% of patients using electrograms with minimal or zero fluoroscopy. Alternatively, HBP can be performed using 3D electroanatomical mapping (EAM), which can significantly reduce fluoroscopy duration and exposure. **Sharma et al.** [41] demonstrated that EAM-guided HBP could be achieved with a conventional 3D mapping system, with the lead course continuously tracked using the 3D system. Once a sharp near-field His signal is identified, intracardiac electrograms and 12-lead ECG can help assess conduction system capture. In patients with underlying bundle branch block or His-ventricle block, mapping of the distal HB may be necessary to achieve complete correction of bundle branch block or to overcome HV block. After confirming lead fixation, the

sheath is gently withdrawn into the high right atrium, providing adequate slack for the lead. Optimal parameters include a unipolar pacing threshold of 1.5-2 mV without atrial over sensing, and an HB current of injury (COI) recorded from the pacing lead electro gram indicates lead fixation in the HB and predicts excellent pacing thresholds. Care must be taken to avoid pinning the tricuspid leaflet into the septum when targeting the ventricular component, using contrast angiography or echocardiography if necessary. Alternatively, the sheath can be moved into the RV apex and pulled back gradually to the target site.

5. Limitations of His Bundle Pacing

Although His bundle technique captures physiological conduction system and results were promising from early studies, one of the current obstacles hindering the widespread adoption of His bundle pacing (HBP) is the technical difficulty in achieving successful implantation with adequate capture threshold. This challenge is more pronounced than in right ventricular pacing (RVP) due to the smaller potential target area for lead placement. As a consequence, the procedural and fluoroscopy times are extended in comparison to RVP. Although operators can overcome the initial learning curve associated with HBP, even experienced operators in the largest published series reported a 27% increase in procedure time (70.2±34 versus 55.0±25 minutes) and a 39% increase in fluoroscopy duration (10.3±6.5 versus 7.4±5.1). [42] Although further advancements in delivery systems and techniques could alleviate this issue, the average implantation time of HBP is expected to remain longer than that of RVP. Another disadvantage of HBP is the need for higher pacemaker energies to achieve His bundle capture compared to RV capture. This often requires selective and nonselective capture thresholds and leads to more rapid battery depletion. In the same large series, the capture threshold was increased compared to RVP (1.30±0.85 V at 0.79±0.26 ms versus 0.59±0.42 V at 0.5±0.03 ms). [42] In a separate report by the same group,

premature generator unit replacement was necessary due to a high threshold in three out of 75 patients undergoing HBP over a period of 4.2±0.4 years. [42] Moreover, an additional three patients in the HBP group in this series required premature generator unit replacement due to a manufacturer advisory notice, and one patient underwent an upgrade to cardiac resynchronization therapy. Finally, His bundle leads tend to be initially less stable than RV leads, leading to a higher incidence of the need for early lead revision (4.2% versus 0% in the Geisinger report).[43] However, this is balanced by low rates of pericardial effusion requiring pericardiocentesis. Although concerns about the performance of HBP following subsequent development of low infra-Hisian block remain, the long-term performance of the leads and generator units following successful implantation appears to be excellent. Ultimately, ongoing and future randomized controlled trials will determine whether the potential clinical benefits of HBP outweigh these disadvantages.

To overcome the above mentioned disadvantages, search for a better physiological site was still undergoing. This seems achievable with the new promising novel technique of Left bundle branch area pacing first demonstrated by **Huang et al** [44] in 2019, which resulted in a more synchronized activation of ventricles.

6. Left Bundle branch pacing

This relatively new technique immediately became a topic of interest amongst cardiologists due to its potential benefits over other pacing modalities. **Huang et al** [44] were first to successfully capture Left bundle branch at relatively low thresholds and give a narrower paced QRS duration providing more synchronous ventricular activation. Left bundle branch is easier to capture due to a wide target area (upto 10mm) with fibers of LBB fanning on the left subendocardium, gives low and stable threshold with no significant sensing issues with beneficial advantage of correcting the distal conduction system disease as the pacing lead

effectively bypasses the diseased segment. In patients undergoing AV junction ablation, LBBP also provides adequate safety margin for ablation as the lead is away from AV node. (Table 2)

Early studies include **Vijayaraman et al** (2019)[12] including 100 patients with indications for pacing were atrioventricular (AV) block 54%, sinus node dysfunction 23%, AV node ablation 7%, cardiac resynchronization therapy 11%, HBP lead failure 7% with left bundle branch block in 24%, right bundle branch block in 25% and intraventricular conduction defect in 8%. Implant success rate was 93%. Paced QRS duration was 136 ± 17 ms. LBB potentials were observed in 63 patients with left bundle branch - ventricle (LBB-V) interval of 27 ± 6 ms. pLVAT was 75 ± 16 ms. Pacing threshold at implant was 0.6 ± 0.4 V @ 0.5 ms and R waves were 10 ± 6 mV and remained stable at median follow-up of 3 months. The lead depth in the septum was approximately 1.4 ± 0.23 cm. The authors concluded LBBAP is feasible in a high percentage of patients and is associated with low and stable capture thresholds during acute follow-up. LBBAP provides a viable alternative in patients with challenging HBP implants, high His thresholds, or conduction disease not corrected by HBP, especially in patients with LBBB. HBP and LBBAP may significantly increase the overall success of physiologic pacing.

Li et al (2019) [45] conducted prospective study including 87 patients (sinus node dysfunction 67.8%; atrioventricular conduction disease 32.2%) undergoing pacemaker implantation. LBBP implantation succeeded in 80.5% (70/87) of patients.LBBP produced narrower electrocardiographic QRSd than did right ventricular septal pacing (113.2 ± 9.9 ms vs 144.4 ± 12.8 ms; $P < .001$) with no major implantation-related complications. The pacing threshold were low (0.76 ± 0.22 V at implantation and 0.71 ± 0.23 V at 3 months), with no loss of capture or lead dislodgment observed.

This technique has become rapidly accepted with various advantages to both RV apical pacing and His Bundle pacing. In a systematic review and meta-analysis by **Zhou et al** (2022) [46] including 7 studies with 867 individuals to compare pacing characteristics of His Bundle Pacing vs. Left Bundle Branch Pacing showed higher implant success rates compared to left bundle branch pacing (LBBP) (relative risk: 1.12, 95% CI: 1.05-1.18; I2 = 60%, P = 0.0003), with lower capture thresholds at implantation (measured in volts per 0.5 milliseconds) (mean difference: 0.63, 95% CI: 0.35-0.90, I2 = 89%, P < 0.0001) and at follow-up (mean difference: 0.76, 95% CI: 0.34-1.18, I2 = 93%, P = 0.0004). HBP recipients also had larger sensed R wave amplitude at implantation (mean difference: 7.23, 95% CI: 5.29-9.16, P < 0.0001) and at follow-up (mean difference: 7.53, 95% CI: 6.85-8.22, P < 0.0001) compared to LBBP recipients However, LBBP recipients had a greater reduction in QRS wave complex at follow-up compared to HBP recipients (mean difference: 6.12, 95% CI: 1.23-11.01, I2 = 0%, P = 0.01). There were no statistically significant differences found in procedure duration, fluoroscopy time, native left ventricular ejection fractions (LVEF), LVEF improvement, native QRS duration, and QRS reduction from the native QRS duration versus paced QRS duration at implantation. Various other studies including small number of patients has shown left bundle branch pacing technique to be highly successful and safe with good lead parameters[47-51] The existing literature has been promising to label left bundle branch pacing as an ideal technique, however still lacks enough data and needs more prospective studies and follow-ups to have a better understanding and experience with its long term effects.

7. Left bundle branch pacing technique

LBBP was first defined by **Huang et al.** [52] as capture of the LBB (left bundle trunk or its proximal fascicles), usually with septal myocardium capture at low output (<1.0 V/0.4 ms).

Technique involves a (1) transvenous access; (2) transseptal placement of the pacing lead into the LV septal subendocardium in the LBB region; and (3) confirmation of capture of the LBB.

Below mentioned Criteria's for LBB capture confirmed by electrical characteristics were described by authors out of which, in clinical practice, patients who meet criteria 1, 2, and at least 1 of latter 3 criteria can be confirmed to have LBB capture.

1. Paced morphology of right bundle branch block pattern

When the lead is placed trans-septally from the right ventricular (RV) septum to LV septal sub-endocardium in the LBB region, the paced QRS morphology changes from an LBBB to a right bundle branch block (RBBB) pattern (Fig), as the LV is activated earlier than the RV. However, the paced morphology could be influenced by the pacing site of the LBB, existing bundle disease, or selective or nonselective LBB capture.

2. Identification of the LBB potential

In patients with non-LBBB during intrinsic rhythm, LBB potentials should always be recorded from the LBBP lead, with the potential to ventricle interval of 20–30ms, to help confirm lead position and the level of conduction block. However, in patients with LBBB, LBB potentials can only be recorded during restoration of left bundle conduction by means of HBP.

3. Pacing stimulus to LV activation time

Pacing stimulus to left ventricular activation time is defined as the interval from the pacing stimulus to the peak of the R wave measured in leads V4-

V6, it reflects the lateral precordial myocardium depolarization time. Stim-LVAT that shortens abruptly with increasing output or remains shortest and constant both at low and high outputs suggests LBB capture,

4. Determination of selective and nonselective LBBP

Selective LBBP, capturing only the LBB as a direct LBB capture sign, can be demonstrated with a discrete local component separate from the stimulus artifact on the unipolar electrogram (EGM) from the LBBP lead.

5. Evidence for direct LBB capture

The interval between the pacing stimulus and the retrograde His potential or anterograde distal LBB potential recorded with an additional lead/catheter during LBBP can be used to confirm LBB capture but it need not be routinely used in clinical practice.

8. Current indications for physiological pacing

Conduction system pacing has three main categories of potential indications. The first category includes conditions where a high burden of ventricular pacing is necessary, such as atrioventricular block (AVB), slowly conducted atrial fibrillation (AF), pacing-induced cardiomyopathy, and atrioventricular nodal ablation (AVNA). The second category is cardiac resynchronization therapy (CRT) for patients with heart failure and bundle branch block (BBB). The third category is sinus node dysfunction (SND), where AV nodal conduction disease may coexist or develop during follow-up. Large registries of international experience have provided a picture of contemporary practice, indicating that AVB and AF are the most common indications.[45] Other potential indications for conduction system pacing include first-degree AVB with narrow QRS, where HBP can be used to shorten AV delay while preserving physiological ventricular activation.

HBP is recommended as class IIa for patients with LVEF between 36% and 50% requiring ventricular pacing (>40% of the time) and as class IIb

for patients with AV block at the level of the AV node (2018 AHA/ACC/HRS).[9]

The potential role of HBP in heart failure is to prevent the development of pacing-induced cardiomyopathy and can be used as an alternative to biventricular pacing (BiVP) in patients with heart failure with LBBB and those with narrow QRS and PR prolongation.

The indications for LBBP are still evolving, but some general guidelines have been proposed. Patients with symptomatic heart failure and LBBB who have failed medical therapy, have reduced ejection fraction (EF), and a prolonged QRS duration (>= 130 ms) may be candidates for LBBP.[53] Patients with an existing cardiac implantable electronic device (CIED) who require an upgrade or replacement of their device may also be considered for LBBP. Patients with non-ischemic cardiomyopathy and LBBB who are candidates for CRT, but may not be ideal candidates for traditional CRT due to anatomical limitations, may also be considered for LBBP. However, the decision to recommend LBBP should be made on an individual basis by a qualified cardiac electro physiologist, as each patient's case is unique.

9. Need for Study

Physiological pacing is a new emerging technique which still lacks substantial data and needs more evidences and experiences from different centers to support its potential benefits. Few Studies also lack echocardiographic features and follow-ups. We hereby conducted a retro-prospective study with an aim to study and compare on follow up of clinical, echocardiographic, ECG and lead parameters of physiological pacing which will increase the knowledge of this novel technique and add to existing data.

MATERIAL AND METHODS

SOURCE OF DATA

The study population consisted of non-consecutive patients meeting inclusion criteria for pacemaker implantation with an initial attempt to perform physiological pacing technique following informed consent from 1st August 2021- 31st July 2022 with follow-up of 6 months till 31st January 2023 at Dayanand Medical College & Hospital.

7.2 METHOD OF COLLECTION OF DATA

INCLUSION CRITERIA:

1. Patients with sympotatic sinus node dysfunction or atrio-ventricular blocks with Class I and IIa Recommendation for pacemaker implantation as treatment of choice according to 2018 ACC/AHA/HRS Guideline on the Evaluation and Management of Patients with Bradycardia and Cardiac Conduction Delay.[32]
2. Patient with Heart failure with reduced ejection fraction with Ejection fraction of <35% with LBBB and QRS duration of ≥ 150 mseconds on GDMT with ≥III NYHA Functional class.

EXCLUSION CRITERIA:

1. Lack of Informed consent
3. Patients with sinus node dysfunction or atrio-ventricular blocks, with Class III recommendation according to 2018 ACC/AHA/HRS Guideline on the Evaluation and Management of Patients with Bradycardia and Cardiac Conduction Delay.[32]
2. Presence of septal scar on Transthoracic echocardiographic assessment.
3. Uncertainty of indication due to probable reversible cause of bradycardia.

4. Patients with current or recent history of severe, progressive, or uncontrolled renal, hepatic, hematological, gastrointestinal, metabolic, endocrine, pulmonary, cardiac, neurological disease.

STUDY DESIGN: A Retro-Prospective study will be conducted at Dayanand Medical College and Hospital, Ludhiana, from August 1, 2021 to September, 2022 with follow-up of 6months till February 28, 2023.

METHODOLOGY: Patients meeting inclusion criteria were analyzed at baseline for NYHA functional class, Electrocardiogram, QRS duration, QRS axis, QRS transition zone, Chest X-ray and transthoracic echocardiographic parameters, septal thickening. Following which Patients underwent physiological pacing technique using 315 His sheath and 3830 pacing lead as an initial method of pacing with an aim to achieve His bundle pacing or Left Bundle branch pacing after full-filling pre-specified criteria's using EP recording system. Post Procedure Electrocardiogram for Paced QRS [ms], QRS axis, QRS transition zone, LVAT, Echocardiograph and lead parameters were measured and any complications were noted. These patients were then followed up after 6 months for reassessment for NYHA functional class, Electrocardiogram, lead parameters, transthoracic echocardiographic parameters and any complications or requirement for lead revision. At end of study Implant success rates was measured along with comparisons between baseline, post-implantation and at 6 months follow-up of clinical status, NYHA class, echo and lead parameters. Data collected was statistically analyzed using appropriate methods.

OUTCOME: It is hypothesized that His and Left bundle branch pacing will be easier to perform with a high successful rate of implantation, Threshold V @ 0.5ms will be in range of 0.5 to 0.8mv,[17] QRS durations will be narrower following procedure with a range of 111-136 ms,[17] with non-significant difference on follow-ups, R wave amplitude will be in range of

9.1 mv-11.99 mv.[17] Physiological pacing can improve clinical profile decrease in functional class and improve echocardiographic parameters with an increase in ejection fraction.

STATISTICAL ANALYSIS: Data will be described in terms of range; mean ±standard deviation (± SD), frequencies (number of cases) and relative frequencies (percentages) as appropriate. Comparison of quantitative variables between the study groups will be done using Student t-test and Mann Whitney U test for independent samples for parametric and non-parametric data respectively. Comparison of quantitative variables within the study groups will be done using paired t-test and Wilcoxon rank sum test for independent samples for parametric and non-parametric data respectively. For comparing categorical data, Chi square ($\chi 2$) test will be performed and exact test was used when the expected frequency is less than 5. A probability value (p value)less than 0.05 will be considered statistically significant. All statistical calculations will be done using (Statistical Package for the Social Science) SPSS 21version (SPSS Inc., Chicago, IL, USA) statistical program for Microsoft Windows.

OBSERVATION AND RESULTS

1. Demographics

- Our study included 42 patients with mean age of study population of 62.76 ± 8.34 years with age group of <50 years constituting 7.1% (3 patients), 51-60 years being most common with 38.2% (16 patients), 61-70 years was 35.7% (15 patient) and > 70 years was 19% (8 patient).
- Our study population showed a male predominance of 83.3% with only 16.7% constituting of female population (as depicted in Figure 1).

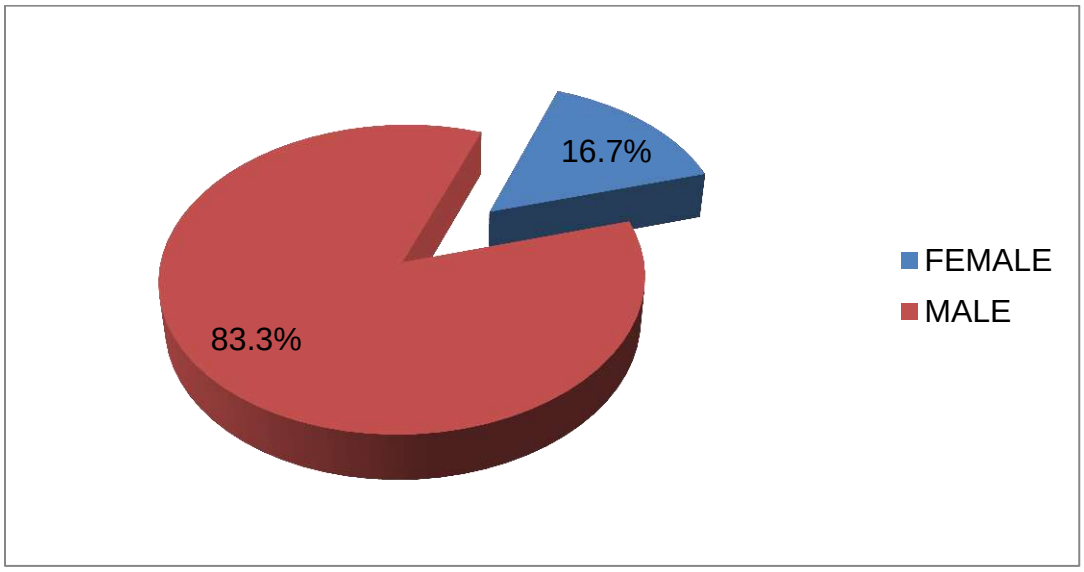


Figure 1: Gender wise distribution

2. CHIEF COMPLAINT

All patients were symptomatic in our study with presenting chief complaint of Syncope in 85.7%, Pre-syncope in 4.8% and Breathlessness in 9.5% as shown in table 1.

Table 1: Presenting complaint of patients

COMPLAINT	No. of cases	Percentage
Syncope	36	85.7%
Pre-Syncope	2	4.8%
Breathlessness	4	9.5%
Total	42	100.0%

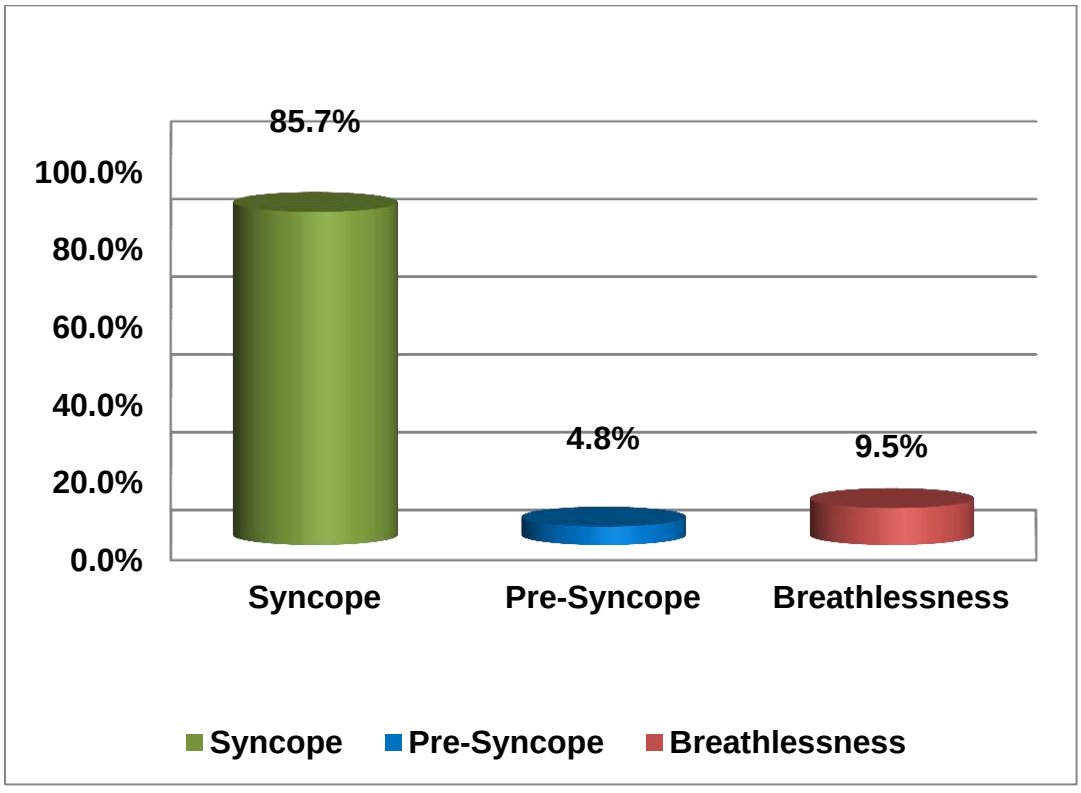


Figure 2: Presenting complaint of patients

3. CO-MORBIDITIES

Morbidity profile of our patient as shown in table 4 depicted Hypertension (35.7%) was most common co-morbidity amongst our study population followed by Diabetes mellitus (26.2%) and Ischemic Heart Disease (26.2%), Hypothyroidism (19%) and Dilated Cardiomyopathy (11.9%) as shown in table 2.

Table 2: Morbidity profile of patients

Co-morbidities	No. of cases	Percentage
Coronary artery Disease	11	26.2%
Hypertension	15	35.7%
Dilated Cardiomyopathy	5	11.9%
Diabetes Mellitus	11	26.2%
Valvular Heart Disease	0	0.0%
Hypothyroidism	8	19.0%

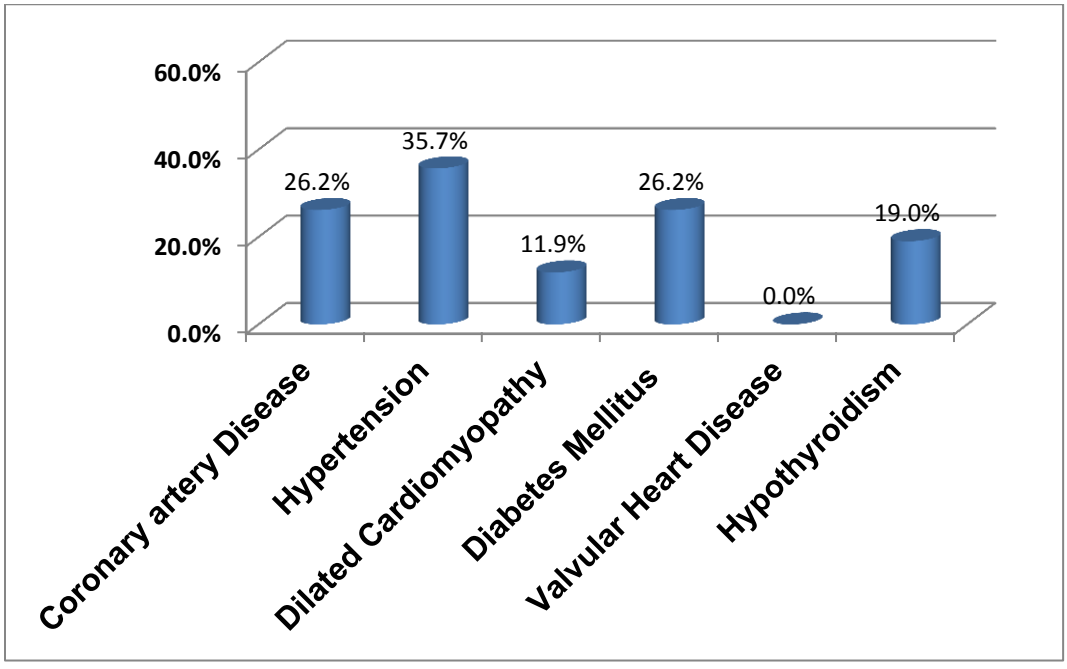


Figure 3: Morbidity profile of patients

4. INDICATION FOR PACING

Out of 42 patients most common cause for Indication for physiological pacing was complete heart block (60%) followed by 2:1 AV block (20%), Sick Sinus syndrome (10%) and Cardiac resynchronization therapy (10%) as shown in table 3.

Table 3 : Distribution of patient according to pacing indication

Indication	No. of cases	Percentage
2:1 AV block	8	20.0%
Complete Heart Block	26	60.0%
Sick Sinus Syndrome	4	10.0%
Cardiac resynchronization therapy	4	10.0%
Total	40	100.0%

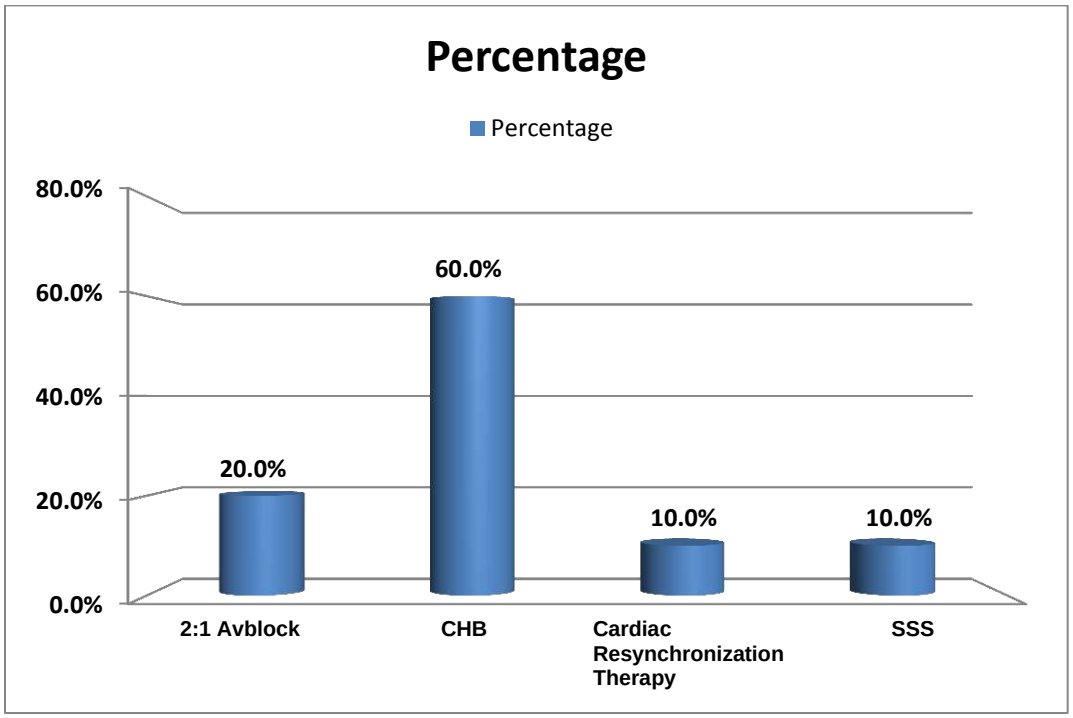


Figure 4: Indication for pacing

5. BASELINE QRS DURATION AND MORPHOLOGY

Baseline QRS duration of our study population was 133.14 ±13.48 milliseconds with normal QRS morphology in 7 patients (17.5%), RBBB in 19%%, LBBB in 35.7%, LAFB in 9.5% and LPFB in 4.8% as shown in table 6.

Table 4: Distribution of study population based on QRS morphology

Baseline QRS Morphology	No. of cases	Percentage
LBBB	15	35.7%
LAF HB	4	9.5%
LPF HB	2	4.8%
RBBB	8	19.0%

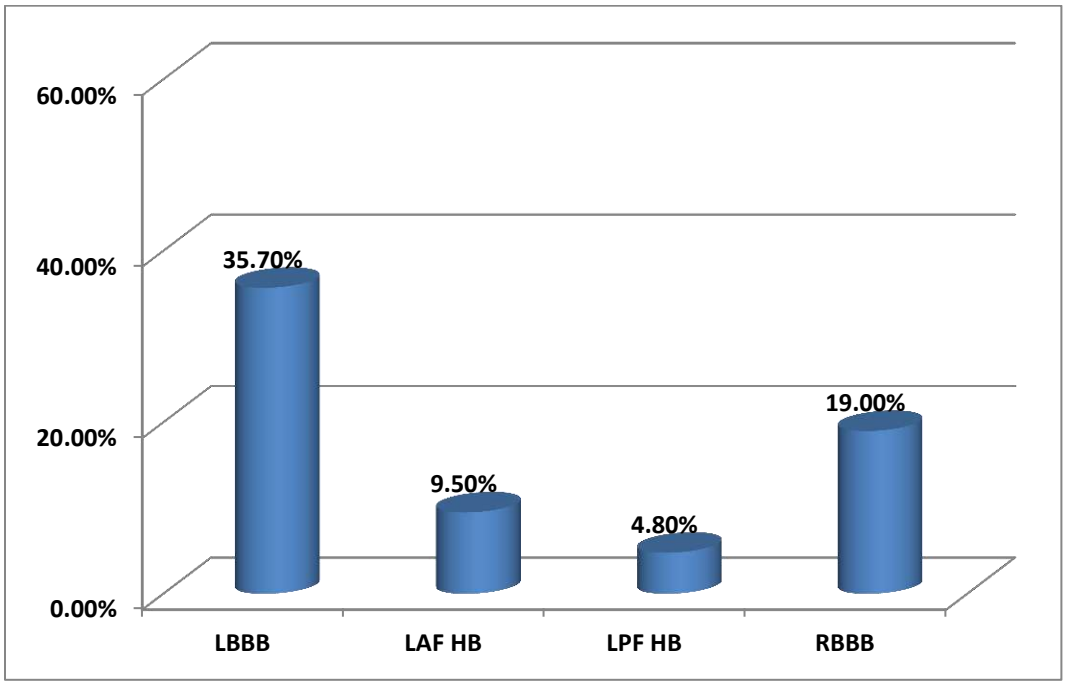


Figure 5: Distribution of study population based on QRS morphology

6. PROCEDURAL CHARACTERISTICS

a. Success rate

Out of 42 patients we were able to achieve a successful physiological pacing in 40 patients (95%) as depicted in Figure 6. LBBAP was achieved in 38 out of 40 (95%) patients and His bundle pacing in 2 out 2 patients (100%).

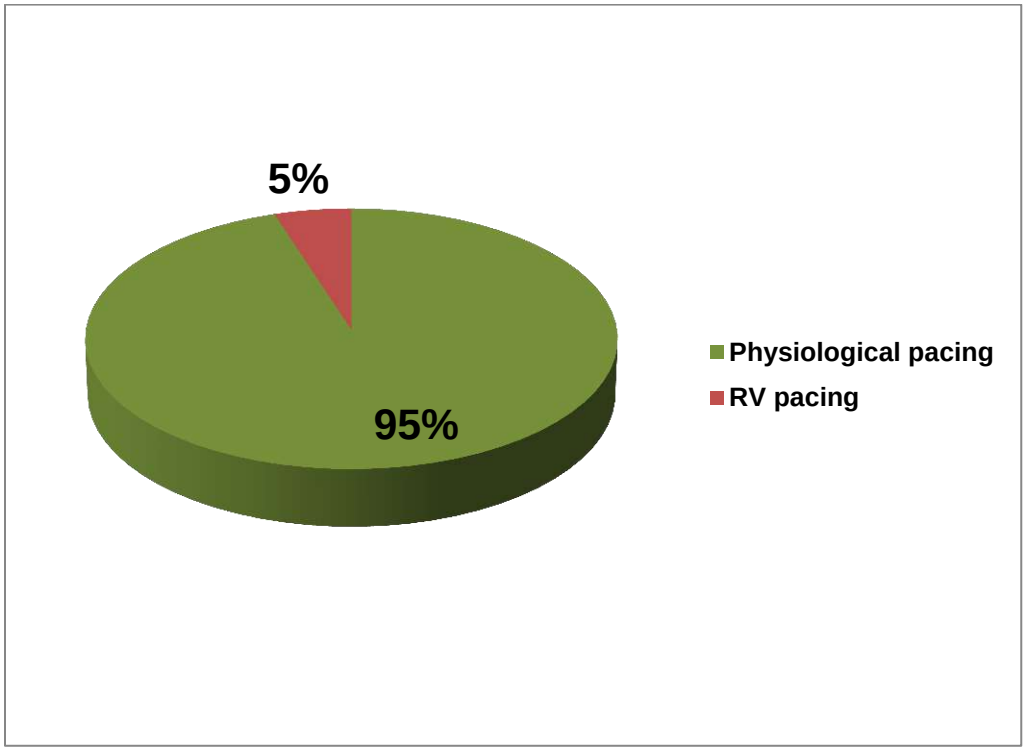


Figure 6: Success Rate

b. Type of Capture

Out of 40 patients with successful physiological conduction system capture, His Bundle capture was achieved in 2 out of 2 patients, Selective LBB pacing was achieved in 22 patients; Left posterior fascicular capture was achieved in 6 patients and Non- Selective LBB capture was achieved in 10 patients as depicted in table 5 (Figure 7).

Table 5: Type of Capture

	n out of 40	**n %**
His Bundle Capture	2	5%
LBB Capture	26	65%
LPF Capture	8	20%
Non-selective	4	10%

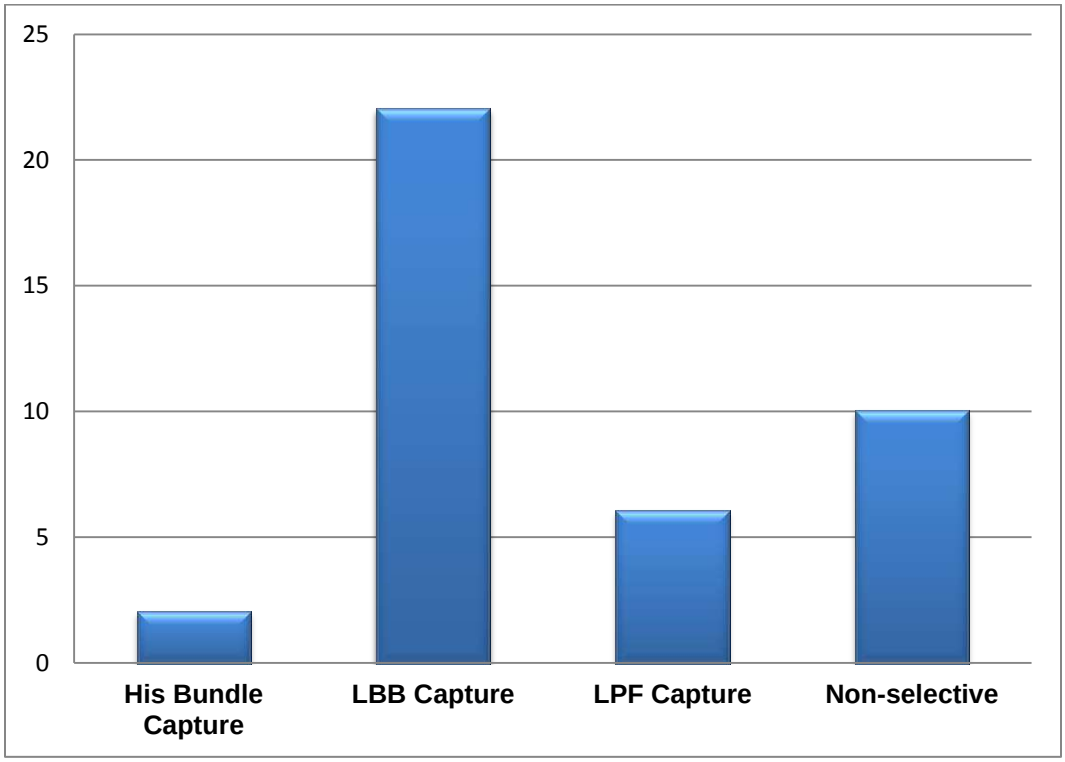


Figure 7: Type of Capture

c. QRS Duration at Implantation

We found that mean QRS duration was significantly reduced post implantation with physiological pacing techniques from baseline (133.14 ±13.48 vs 111.83±14.53;t 8.697; p-value 0.001) as depicted in Table 6.

Table 6: Comparision of QRS duration at Baseline and Post Implantation

	Before		At implantation				Difference	
QRSd	Mean	SD	Mean	SD	t value	p-value	Mean	SD
(in msecs)	133.1	13.4	111.8	14.5	8.697	0.001	21.31	15.88

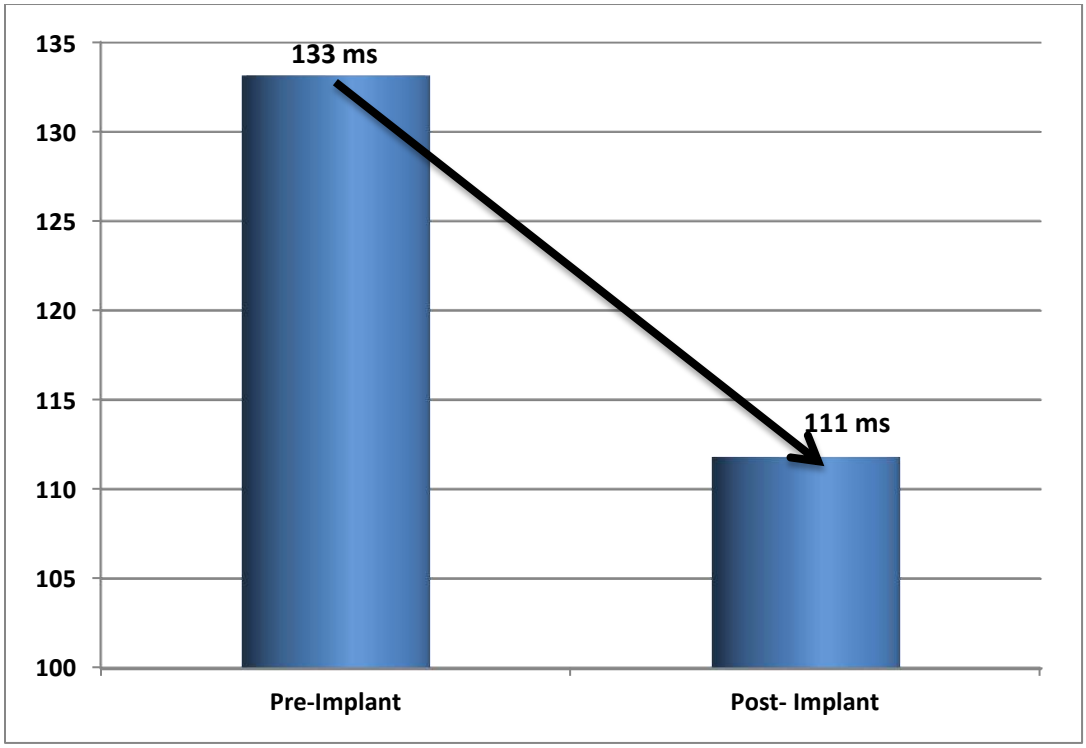


Figure 8: Comparision of QRS duration at Baseline and Post Implantation

d. PACING PARAMETERS

We were able to achieve a low mean capture threshold (0.66±0.18V/0.5msec) at implantation amongst our study population with a Stim-LVAT at 5V/0.4msec of 72.79±12.12 msecs. Mean QRS duration was 111.83±14.53 msecs. Mean Pacing Impedance was 738.19±113.37Ω and sensed R-wave amplitude was 10.10±2.08mv as depicted in table 7.

Table 7: Pacing Parameters at Implantation

Parameters	Minimum	Maximum	Mean	Std. Deviation
1. Stim-LVAT (at 5 V/0.4 ms)	65	90	72.79	12.12
2. Capture threshold, (V/0.5 ms)	0.4	1	0.6	0.18
3. Paced QRSd, (in m sec)	98	132	111.83	14.53
4. Pacing impedance, (in Ω)	560	980	738	113
5. R wave amplitude, (in mV)	3.50	12.50	10.10	2.08
6. Anodal Capture threshold (in V)	1.00	2.20	1.51	0.43
7. Transition zone	2.00	4.00	2.86	0.68

7. Comparison at 6 months of Clinical outcome with NYHA Functional Class

Out of 42 patients 11 patients (26.2%) were in NYHA class I, 7 patients (16.7%) had class II symptoms, 18 patients (42.9%) had class III symptoms and 6 patients (14.3%) were admitted with NYHA class IV symptoms. Our Study showed a decrease in functional class from NYHA IV→III in all 6 patients, with Physiological pacing and optimized guideline directed medical therapy at 6 months of follow-up and had 0% of re-hospitalization for Heart failure or new onset AF till 6 months. (as depicted in Table 8)

Table 8: Comparison of NYHA functional class at baseline and 6 months

	AT BASELINE	AT 6 MONTHS	
FUNCTIONAL CLASS	No. of cases	Change in Functional class	No. of cases
I	11	I	11
		< I	0
II	7	I	1
		II	6
		<II	0
III	18	<II	0
		II	10
		III	8
IV	6	<III	0
		III	6
		IV	0
TOTAL	42		42

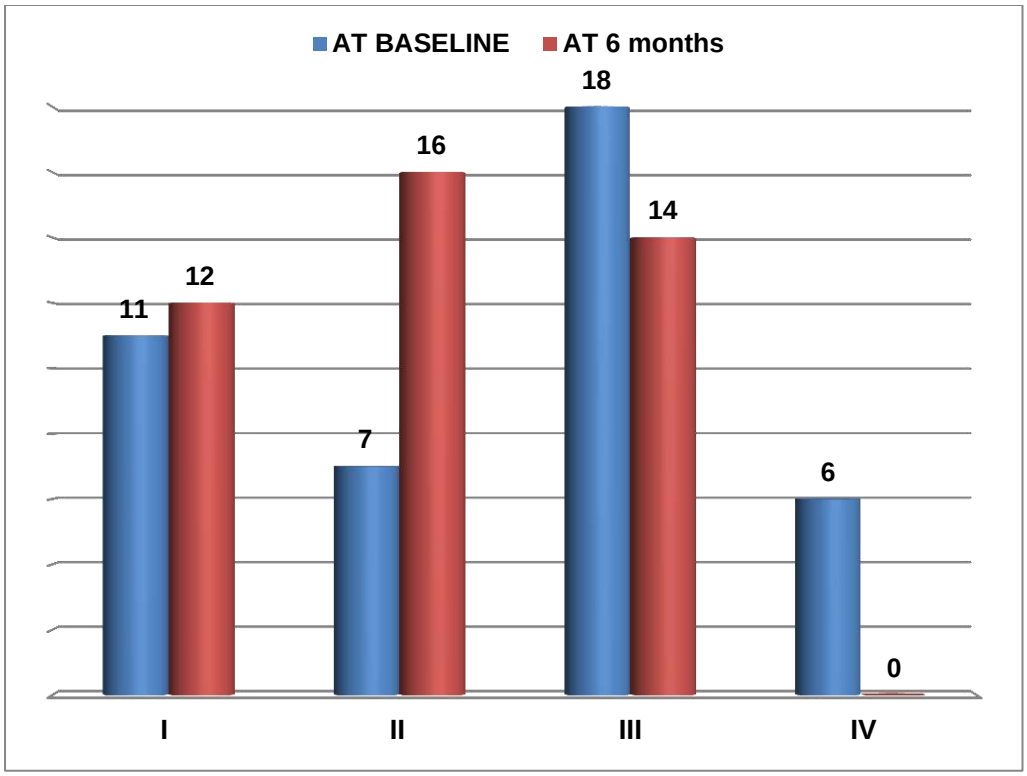


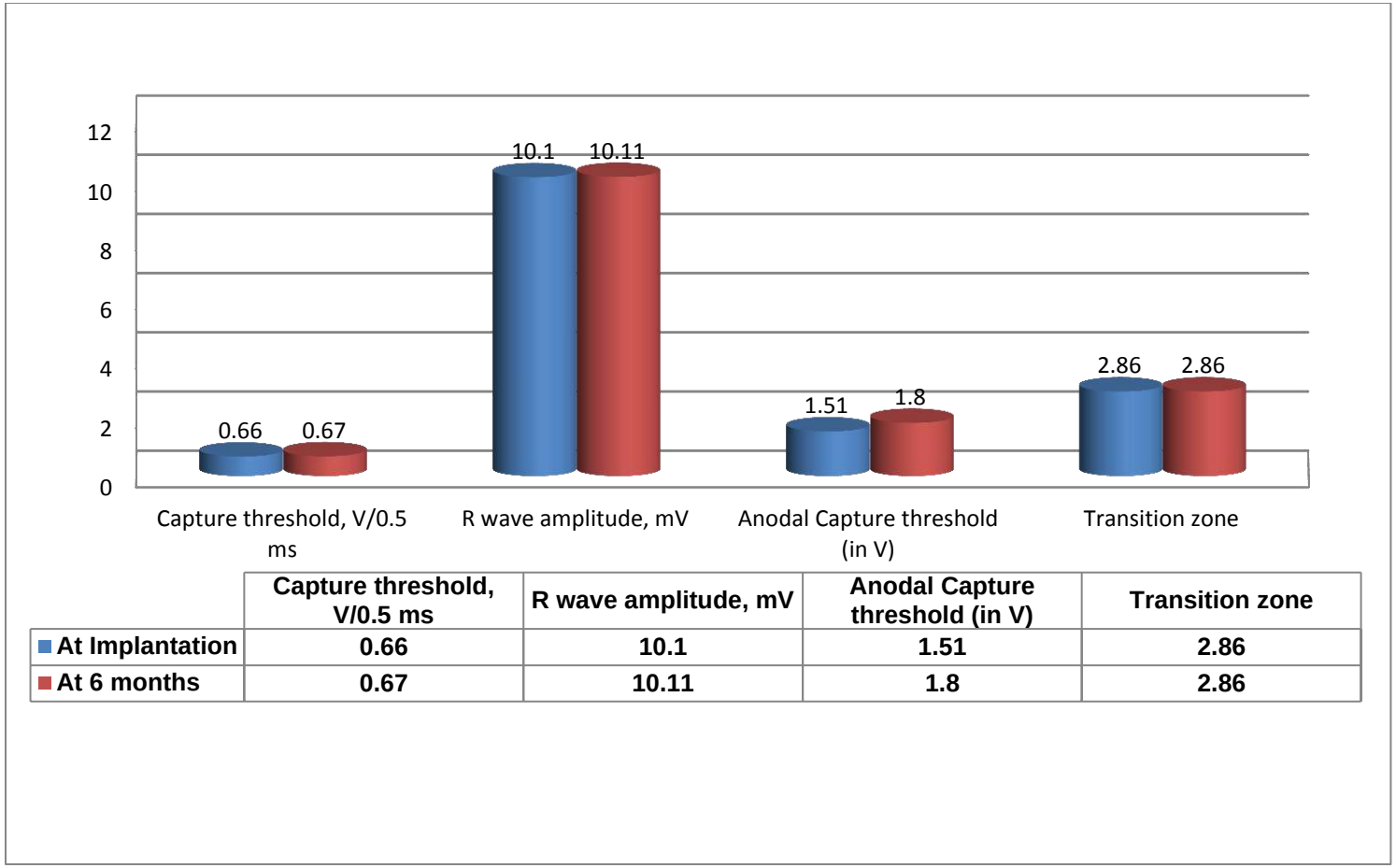
Figure 9: Comparison of NYHA functional class at baseline and 6 months

8. Comparison between pacing parameters at Implantation and at 6 months

We found that pacing lead parameters were statistically similar on short term follow-up at 6 months as depicted in table 9 ; (Figure 10-12) except pacing impedance which decreased from 738.19±113.37 Ω to 608.98±52.75 Ω; t= 6.795;p value=0.001. Stim-LVAT was 72.79±12.12 msecs vs 73.57±10.02 msecs; t -1.209; pvalue=0.234 at 6 months. Capture threshold was found to be almost same 0.66±0.18 vs 0.67 ±0.17; t value -2.218; p value= 0.032. Values of sensed R wave amplitude were 10.10±2.08mV vs 10.11 ±1.47mV; t value 0.036;p value=0.971. Mean QRS duration was slightly increased from 111.83±14.53msecs vs 115±10.86 msecs;t value -3.123; p value 0.003. Mean QRS remained narrow on comparison with baseline at 6 months of follow up as shown in graph 12.

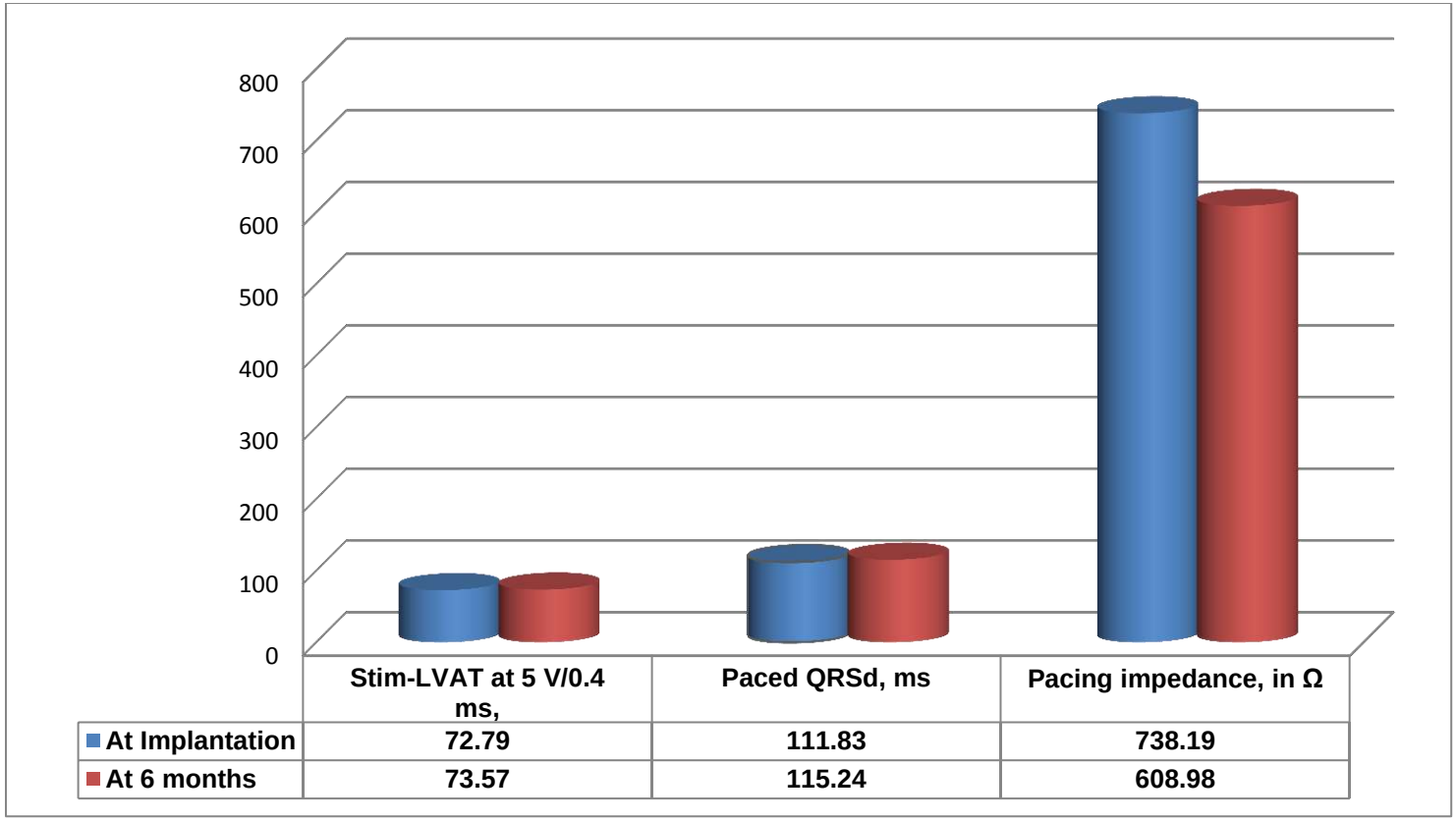
Table 9: Comparison of pacing parameters at implantation and at 6 months follow-up

PARAMETERS	At implantation		At 6 month		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
Sti-LVAT at 5 V/0.4 ms,	72.7	12.1	73.5	10.02	-1.209	0.234	-0.79	4.21
Capture threshold, V/0.5 ms	0.6	0.18	0.6	0.1	-2.218	0.032	-0.01	0.04
Paced QRSd, ms	111.8	14.5	115.2	10.8	-3.123	0.003	-3.40	7.06
Pacing impedance, Ω	738.1	113.3	608.9	52.75	6.795	0.001	129.21	123.24
R wave amplitude, mV	10.1	2	10.1	1.47	-0.036	0.971	-0.01	2.11



	Capture threshold, V/0.5 ms	R wave amplitude, mV	Anodal Capture threshold (in V)	Transition zone
At Implantation	0.66	10.1	1.51	2.86
At 6 months	0.67	10.11	1.8	2.86

Figure 10: Comparison of pacing parameters at implantation and at 6 months follow-up



	Stim-LVAT at 5 V/0.4 ms,	Paced QRSd, ms	Pacing impedance, in Ω
At Implantation	72.79	111.83	738.19
At 6 months	73.57	115.24	608.98

Figure 11: Comparison of Lead Parameters at Implantation and at 6 months

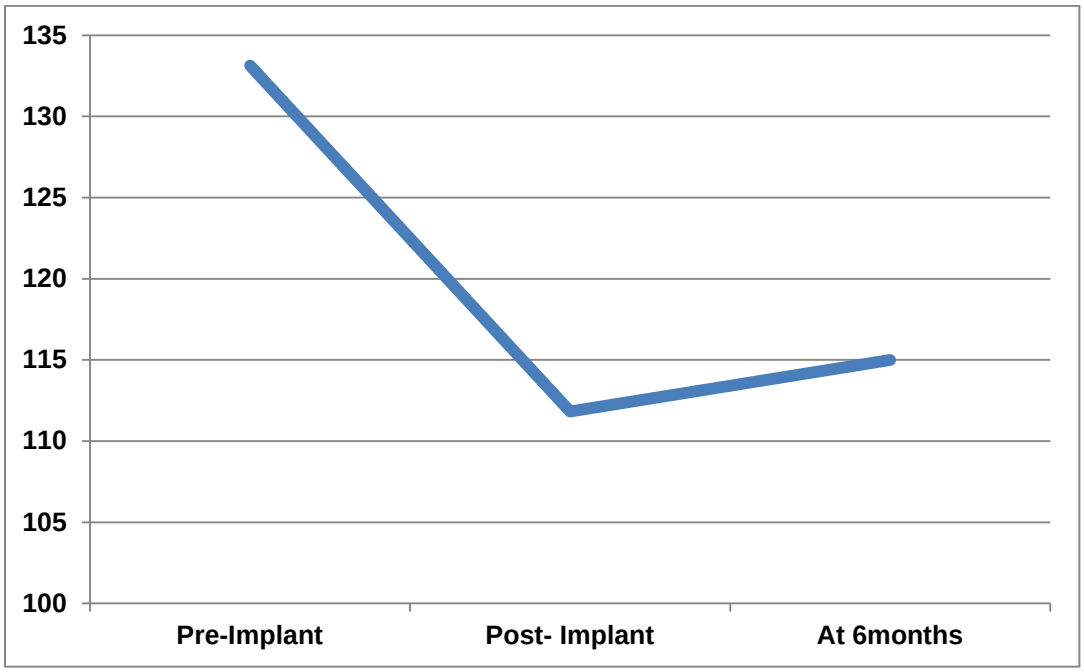


Figure 12: Comparison of mean QRS Duration (in msecs) Pre-implant, Post-Implant and at 6 months of follow up

9. ECHOCARDIOGRAPHIC PARAMETERS

a. Comparison of 2D transthoracic echocardiographic parameters between pre-implantation and post- implantations (48 hours) was done in all patients. Stroke volume (67.62±16.98 ml vs 68.07±16.84ml; t value-1.492;p-value=0.143) and Ejection fraction 46.70±11.14% vs 47.38±10.33%;t value -2.728;p value=0.009) was slightly increased and SPWMD (117.67 ±30.37 vs 114.67±26.64;t value=2.047;p value=0.047) was decreased. These findings were more evident in 4 patients with pacing indication of cardiac resynchronization therapy (mean EF-20.85%±1.9% vs 22.75±2.5%). There was no change in grade of TR or MR in patients post implantation and minimal pericardial effusion was seen in 2 patients. Lead depth was measured in all patients and was found to be 10±2 mm.

   Various other echocardiographic parameters remained same post-implantation as shown in table 10.

Table 10: Comparison of 2D transthoracic echocardiographic parameters between pre-implantation and post- implantations (48 hours)

	Pre- implantation		Post-Implantation 48 hours		T	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
LA size (in mm)	36.2	4.8	35.5	5.0	1.066	0.293	0.69	4.20
RA size (in mm)	29.2	5.3	28.9	5.4	0.565	0.575	0.31	3.55
RVID (in mm)	27.5	3.1	26.8	3.1	1.578	0.122	0.64	2.64
IVST (D) (in mm)	7.2	0.8	7.6	0.7	-2.101	0.042	-0.33	1.03
IVST (S) (in mm)	7.4	1.0	7.5	1.1	-0.313	0.756	-0.05	0.99
LVID (D) (in mm)	50.9	5.1	49.7	5.1	1.648	0.107	1.26	4.96
LVID (S) (in mm)	38.4	7.3	37.0	7.7	1.566	0.125	1.40	5.81
LVPW (D) (in mm)	6.8	0.9	7.3	1.1	-2.708	0.010	-0.55	1.31
LVPW (S) (in mm)	7.8	0.9	7.6	1	1.185	0.243	0.19	1.04
SPWMD (in msecs)	117.6	30.3	114.6	26.6	2.047	0.047	3.00	9.50
LVDV (in ml)	148.4	22.7	146.0	19.7	2.598	0.013	2.33	5.82
LVSV (in ml)	81.5	28.1	79.2	24.6	2.065	0.045	2.26	7.10
SV (in ml)	67.6	16.9	68.0	16.8	-1.492	0.143	-0.45	1.97
EF%	46.7	11.1	47.3	10.3	-2.728	0.009	-0.68	1.62

Table 11: Comparison of 2D transthoracic echocardiographic parameters between pre-implantation and post- implantations (48 hours) for valvular regurgitation

Valvular regurgitation	Severity	Baseline		At 48hours	
		No. of cases	Percentage	No. of cases	Percentage
MR	Mild	3	7.10%	3	7.10%
	Moderate	3	7.10%	3	7.10%
	None	36	85.70%	36	85.70%
AR	Mild	2	4.80%	2	4.80%
	None	40	95.20%	40	95.20%
TR	Mild	11	26.20%	9	21.40%
	Moderate	6	14.30%	6	14.30%
	None	24	57.10%	26	61.90%
	Severe	1	2.40%	1	2.40%
PR	Mild	1	2.40%	1	2.40%
	None	41	97.60%	41	97.60%

b. Comparison of Echocardiographic parameters pre-implantation and at 6 months of follow-up.

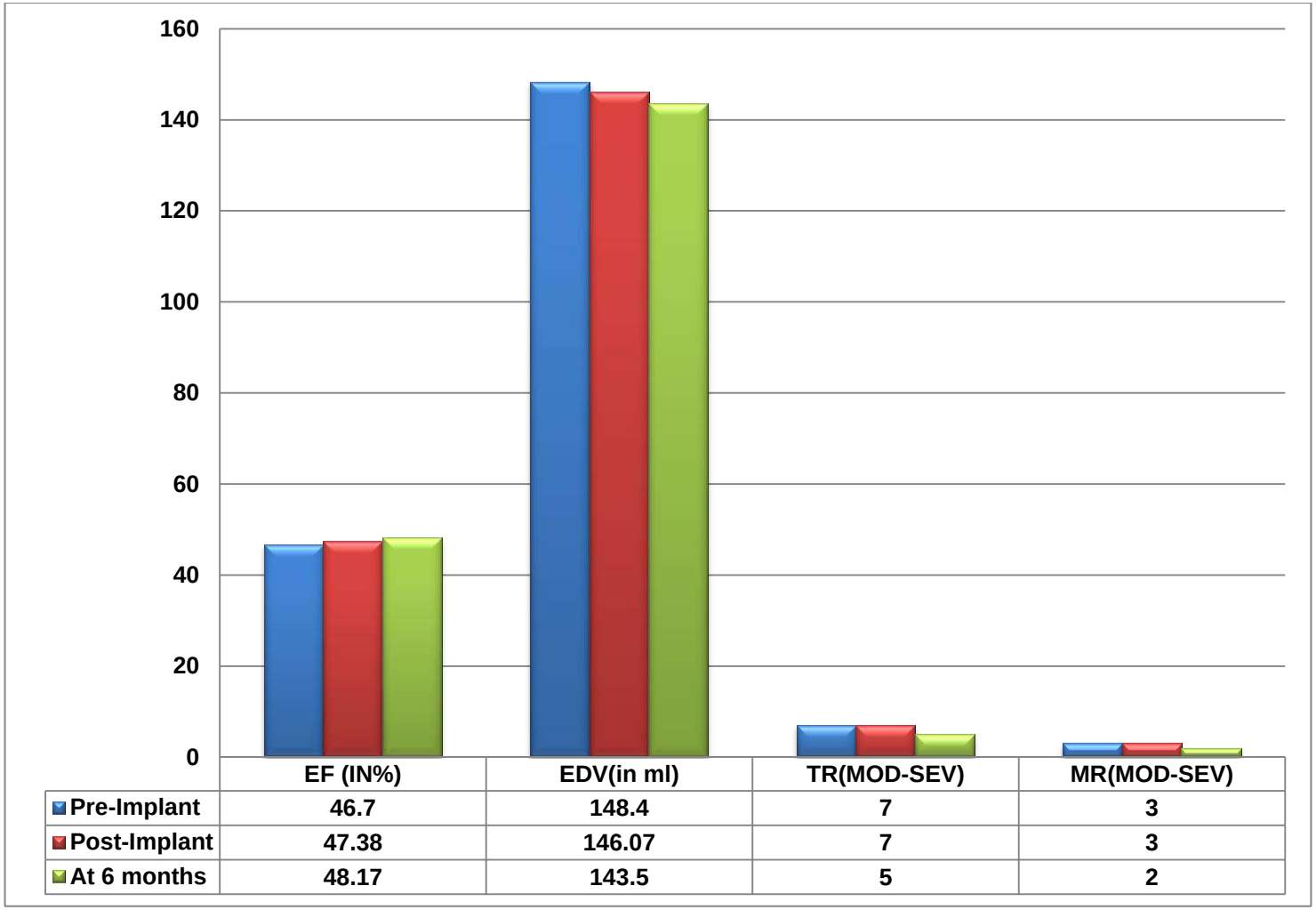
On follow up at 6 months we found statistically significant improvement in Ejection fraction 46.70±11.14% vs 48.17±9.53%; t value -3.226;p value= 0.002. There was no macro lead dislodgement at 6 months of follow up and no development or significant increase of grade of TR or MR.

Table 12: Comparison of 2D transthoracic echocardiographic parameters between pre-implantation and post- implantations (48 hours)

	Pre- implantation		**At- 6 months**		**T**	**p-value**	**Difference**	
	Mean	**SD**	**Mean**	**SD**			**Mean**	**SD**
LA size (in mm)	36.2	4.8	35.7	4.6	1.047	0.301	0.48	2.95
RA size (in mm)	29.2	5.3	29.4	5.3	-0.356	0.724	-0.17	3.04
RVID (in mm)	27.5	3.1	27.0	3.1	1.097	0.279	0.48	2.81
IVST (D) (in mm)	7.2	0.8	7.6	0.8	-2.243	0.030	-0.36	1.03
IVST (S) (in mm)	7.4	1.0	7.2	1.0	1.502	0.141	0.21	0.92
LVID (D) (in mm)	50.9	5.1	49.9	5.0	1.434	0.159	1.07	4.84
LVID (S) (in mm)	38.4	7.3	36.9	7.4	1.748	0.088	1.50	5.56
LVPW (D) (in mm)	6.8	0.9	7.1	1.0	-1.874	0.068	-0.31	1.07
LVPW (S) (in mm)	7.8	0.9	7.86	1.0	0.154	0.878	0.02	1.00
SPWMD (in msecs)	117.6	30.3	114.8	26.3	1.620	0.113	2.81	11.24
LVDV (in ml)	148.4	22.7	143.5	18.1	3.361	0.002	4.90	9.46
LVSV (in ml)	81.5	28.1	76.7	22.2	2.884	0.006	4.79	10.75
SV (in ml)	67.6	16.9	68.2	16.2	-1.097	0.279	-0.62	3.66
EF%	46.7	11.1	48.1	9.5	-3.226	0.002	-1.47	2.95

Table 13: Comparison of 2D transthoracic echocardiographic parameters between pre-implantation and at 6 months for valvular regurgitation

Valvular regurgitation	Severity	Baseline		At 6months	
		No. of cases	Percentage	No. of cases	Percentage
MR	Mild	3	7.1%	4	9.5%
	Moderate	3	7.1%	2	4.8%
	None	36	85.7%	36	85.7%
AR	Mild	2	4.8%	2	4.8%
	None	40	95.2%	40	95.2%
TR	Mild	11	26.2%	11	26.2%
	Moderate	6	14.3%	4	9.5%
	None	24	57.1%	26	61.9%
	Severe	1	2.4%	1	2.4%
PR	Mild	1	2.4%	1	2.4%
	None	41	97.6%	41	97.6%



	EF (IN%)	EDV(in ml)	TR(MOD-SEV)	MR(MOD-SEV)
Pre-Implant	46.7	148.4	7	3
Post-Implant	47.38	146.07	7	3
At 6 months	48.17	143.5	5	2

Figure 13: Comparison of 2D transthoracic echocardiographic parameters between pre-implantation, post- implantations (48 hours) and at 6 months

10. Complications

a. Early

Out of 42 patients, we experienced difficulty to capture a physiological site for pacing in 2 patients, who demonstrated a high pacing threshold and high impedance (>1000 Ω) at multiple septal sites using 315 His Sheath and 3830 select secure lead. 1 patient was managed with conventional RV apical pacing (QRS duration 130msec, threshold 0.8V, Impedance 780Ω) and other patient received RVSP at acceptable parameters (QRS duration 126msec, threshold 0.8V, Impedance 880Ω). LBB potential could not be recorded in both these 2 patients. Lead revision was done in 3 patients out of whom successful LBB capture was achieved in one patient on 2nd attempt. Macro-lead dislodgement took place in 1 patient while slitting of sheath, however successful re-implantation was done at similar parameters. There were no incidences of lead perforation, pneumothorax, pocket hematomas and pacemaker infections .

b. Late

There were no late complications noted on follow-up till 6 months. On pacemaker interrogation no patient had any major increase in impedance or threshold, failure to capture or sensing, pacemaker infections.

Table 14: Complications

PROCEDURAL COMPLICATIONS	No. of cases	Percentage
Macro Lead dislodgement	1	2.4%
Micro Lead dislodgement	2	4.8%
Lead perforation	0	0%
Persistent RBB injury	0	0.0%
Pericardial effusion	0	0.0%
Pacing system infection	0	0.0%
Pocket hematoma	0	0.0%
Pneumothorax/hemothorax	0	0.0%

DISCUSSION

We conducted a retro-prospective single- center study for duration of one year with an aim to study effects of physiological pacing and its short-term clinical outcomes at 6 months of follow-up. A total of 42 patients were included in duration of this study for various indications of physiological pacing out of which successful physiological pacing was performed in 40 patients [LBBP 38 (95%) and HBP 2(100%)].

1. Demographics

A total of 42 patients were included during the duration of this study, out of which all patients (42/42; 100%) were successfully followed up at 6 months with 0% drop-out rate, death or failure to follow-up. The mean age of all patients included in our study who enrolled for study 62.76±8.34 years. This has been similar with findings of **Shunmuga et al.** [54] including 99 patients for left bundle pacing with mean age of 62.6 ± 13.1 years in Indian population and **Li et al.** [45] including 87 patients with mean age of 63.8±11.4 years in Asian population. The mean age was higher amongst the western population as reported by **Vijayaraman et al** [12] with mean age 75.6 ± 13.1 years among 100 patients requiring pacing.

2. Gender distribution

Our study was Male predominant with Male to Female ratio of 5:1. Total Males were 85% (35 patients) and Females were 15% (7 patients). Other studies have also shown a male predominance of 69% by **Vijayaraman et al**[12] and 59% by **Shunmuga et al.** [54] Our study has a comparatively higher male predominance as an incidental finding and smaller sample size. Previously reported literatures have also shown difference in incidences of type of pacemaker used for females with lower incidences of AV blocks and higher incidences of SND as primary indication when compared with males due to unclear mechanism and to some extent by the effects of sex hormones on autonomic tone modification and on

electrophysiological properties but overall no significant differences has been reported for incidence of Implantable cardiac devices needed between male and females.[55]

3. Co-Morbidities

In our study co-existing morbidities were Hypertension (35.7%), Diabetes Mellitus (26.2%), Coronary artery disease (26.2%), Dilated Cardiomyopathy (11.9%) and Hypothyroidism (19%). Associated chronic illnesses amongst patient with bradyarrythmias requiring permanent pacemaker is well reported out of which Coronary artery disease and Diabetes mellitus is one of the most common ones which can also be an independent factor due to increasing age.[1] Associated chronic illness amongst our study population is also due to increasing age and interplay of other risk factors leading to early degeneration and fibrosis of conduction system like Chronic Coronary syndrome, Diabetes mellitus and Hypothyroidism. However our study reports a lesser incidence of chronic illnesses which can be an incidental finding due to a smaller sample size and relatively younger population with majority of age group <60 years constituting 57.5% of our study population.

4. Indication for Pacing

Physiological pacing like HBP and LBBP is recommended as class IIa for patients with LVEF between 36% and 50% requiring ventricular pacing (>40% of the time) and as class IIb for patients with AV block at the level of the AV node (2018 AHA/ACC/HRS).[9] Out of 42 Patients we had all symptomatic patients with presenting complaint of syncope in 85%, pre-syncope in 5% and breathlessness in 10% with various indications for pacing - 2:1 Atrio-ventricular block (20%), complete heart block (60%), Sick Sinus syndrome (10%) and Cardiac resynchronization (10%). Previous studies also include patients with atrial fibrillation with AV node junction ablation and HBP lead failure needing lead revision.[12,45,54]

5. ECG characteristics at baseline

Minimum HR recorded in our study was 46.63 ± 11.61 beats per min with a mean QRS duration of 133.14 ± 13.48 msecs and underlying LBBB in 35.7% and RBB in 19% population. These findings have been similar with other studies for baseline characteristics of patients indicated for physiological pacing.[12, 45, 54]

6. Success rate

We included 42 non-consecutive patients with various indications for physiological pacing out of which successful physiological pacing was done in 40 patients with success rate of 95.2%. Our findings are in concordance with various other prospective studies which have shown success rates of 80%-97%.[12, 45, 49, 54] Since its initial description and feasibility of physiological pacing, the technique has recently evolved over past 5 years with help of advances in sheath delivery system, electrophysiological mapping and pacing leads. Left bundle branch pacing is also proven to be technically easier than His Bundle pacing due to a larger target. **Vijayaraman et al** [12] reported a success rate of 93% amongst 100 patients, **Li et al** [45] included 87 patient with a success rate of 80.5%. **S Ponnsuamy et al** [54] included 99 patients and reported a success rate of 94%.

7. Procedural characteristics

A total of 42 patients included in this study for various indications of physiological pacing underwent either His bundle pacing or Left bundle branch pacing attempt with success rates of 95.2%.We observed that all criteria's for Left bundle branch pacing cannot be met and paced morphology of right bundle branch block pattern and constant Stim-LVAT on low and high threshold were 2 criteria's always met (100%) with other criteria of LBBB potential recorded in 24 patients (57%), similar study by **Vijayaraman et al** [12] demonstrated recording of LBB potentials in 63% of

patients. These findings can be explained by prevalence of baseline LBBB, complete heart block without an escape rhythm, suboptimal potentials or cardiomyopathy related fibrosis. Lead implantation could not be done in 2 patients due to possible underlying fibrosis or scar. This has been a relatively new technique with first experience and study at our center with small sample size.

8. Pacing parameters with follow-up

A.QRS duration

Physiological pacing technique helps in stimulating the natural conduction system or peri-conduction area which has superior electrophysiological properties when compared to myocardium or purkinje fibers. This leads to a synchronized and a rapid ventricular contraction of the heart which is evident by a narrower QRS duration. **In our study** we found a highly significant reduction in QRS duration (133.14±13.48 msecs vs 111.83±14.53 msecs; t value 8.697; p<0.001). The QRS duration remained stable on 6 months follow- up **(111.83±14.53 msecs vs 115.24 ± 10.86 msecs; t value -2.787; p =0.009).** These findings are in concordance with similar prospective studies showing significant reduction of QRS duration which remain stable on short term follow up. **Ponnsuamy et al** [(54)] included 99 patients (atrioventricular (AV) block 43%, cardiac resynchronization therapy 44%, and AV node ablation 4%) and achieved 94% acute success rate for LBB pacing with reduction of QRS from 144.38 ± 34.6 at baseline to 110.8 ± 12.4 ms after LBBP (p < 0.0001) which held stable till mean follow-up of 4.8 months.

However, **Vijayaraman et al** [12] including 100 patients (atrioventricular (AV) block in 54%, sinus node dysfunction in 23%, AV node ablation in 7%, cardiac resynchronization therapy in 11%, HBP lead failure in 7% as pacing indication) had baseline QRS duration of 133 ± 35 ms. LBB pacing was successful in 93% with paced QRS duration of 136 ± 17 ms. The

authors explained these findings on the basis of a prospective study by **Mafi-Rad M et al** [56] which studied feasibility and acute hemodynamic effect of left ventricular septal pacing by transvenous approach through the interventricular septum which concluded that LV septal pacing has a narrower QRS and acute hemodynamic benefits when compared to RV septal. **Mafi-Rad M et al** [56] reported QRS duration of 144 ± 20 ms by LVS pacing which when compared to findings of Vijayraman et al 136 ±17 ms was higher. Similarly, work by **Li et al** (45) showed a slight increase of QRS duration from baseline (105.5 ± 22.2 ms vs 113.2 ± 9.9 ms ($P < .05$), However this was significantly lower than RV septal pacing (113.2 ± 9.9 ms vs 144.4 ± 12.8 ms; $P<.001$). The duration of QRS complex on the surface ECG can be used as an indirect measure of ventricular activation time. Notably, left bundle branch pacing (LBBP), which typically results in a right bundle branch block, the mean QRS duration in our study was < 120 ms. This suggests that retrograde activation of the right bundle with pacing or connections between the main right and left bundles may have occurred. Additional research is necessary to better understand the mechanism behind relatively short paced QRS durations observed with this technique.

B. Pacing thresholds-

Physiological pacing requires determining the pacing threshold, which is the minimum energy needed to stimulate the myocardium. In left bundle branch pacing (LBBP), the threshold may be higher than traditional RV pacing due to anatomical complexity and the smaller size of the left bundle. Careful selection of pacing parameters and device programming is essential to ensure effective pacing and avoid complications. Factors like lead placement, pacing site, and patient characteristics influence pacing thresholds. Regular evaluation is crucial to optimize device function and patient outcomes. In this retro-prospective study conducted at a single center, we achieved a low pacing thresholds (0.65±0.17 V @ 0.5 msecs),

which aligns with the findings of other comparable studies. **Vijayaraman et al** [12] documented a pacing threshold of 0.6 ± 0.4 V, **Li et al** [45] reported a threshold of 0.76 ± 022 V, and Zhang et al[49] reported a threshold of 0.68 ± 02 V, with an overall agreement of a threshold below 1V.Pacing thresholds in physiological pacing are crucial for effective and safe cardiac pacing. Close monitoring of pacing thresholds is necessary to avoid potential complications and optimize pacing efficacy in patients undergoing physiological pacing. We found that these pacing thresholds remained practically static on short term follow-up at 6 months (0.66±0.18 V vs 0.67± 0.17 V;p<0.)

C.LVAT

Left ventricular activation time or LVAT reflects the amount of time taken for the electrical signal to spread through the left ventricle and measured as time interval from the pacing stimulus to peak of R wave in V5 or V6. The LVAT also determines the depth of lead engagement as it may be prolonged in patients with intraventricular conduction defects and ischemic cardiomyopathy with significant scar. LVAT of less than 80 msecs is usually suggestive of Left Bundle branch pacing. We report a LVAT of 72.79±12.12 msecs which has been comparable as reported by **Vijayaraman et al.**[12] (75 6±16 msec), **Ponnusamy et al** [54] (75±16 msec).

D. Impedance

Monitoring the impedance on follow-up visits is an important aspect of managing patients who undergo left bundle branch pacing (LBBP). The impedance may change over time due to a variety of factors, including lead displacement, tissue healing, and changes in the surrounding tissue. A decrease in impedance may indicate lead displacement, which can occur as a result of tissue healing or movement of the heart within the chest. In our study we observed an impedance of 738.19±113.37Ω which

has been in similar range with other studies. This impedance is however dropped to 608.98 ± 52.75 Ω on 6months of follow up ($p<0.01$). This fall in impedance can be explained due to a lead-to-tissue contact, which also results in improved electrical conductivity and lower resistance to the pacing current. A decrease in impedance with lower thresholds for achieving capture is due to lead-to-tissue contact this also reduces the amount of energy required for successful pacing and help in reduction of battery consumption and prolonging the life of the pacing device. **Li et al.**[45] reported an impedance of 700.14±134.87Ω at implantation which reduced to 472.40 ± 91.41 Ω at 3 months of follow up. We recommend regular follow-up visit, to monitor impedance changes and ensure the effectiveness and safety of LBBP. The frequency of follow-up visits can vary depending on the patient's clinical status and individual factors, but generally, it is recommended to have follow-up visits every 6 to 12 months after the initial implantation of the pacing system.

E. Sensed R- wave amplitude

Physiological pacing technique involves placing of lead on conduction system; this provides higher sensed R wave amplitude which is optimal for timing of the pacing signal. Higher R wave amplitudes in LBB pacing also indicates proper lead placement, optimal timing of the pacing signal, and effective pacing capture. These factors can also improve cardiac function and reduce symptoms of heart failure by providing effective and synchronous ventricular contraction. In our study we observed that mean R wave amplitude was 10.10 ± 2.08 V which remain near constant on at 6 months follow-up (10.11 ± 1.47 V). These findings have been in concordance with **Li et al.** [45] which reported R wave Amplitude of 11.99 ± 5.36 V and 16.90 ± 6.78 V on 3 months follow up. **Ponnsuamy et al**. [54] reported R wave of 14.14 ± 7.19 mV at implantation and 13.68 ± 5.2 mV on Follow-up of 1-12 months with p value= 0.199.

8. Echocardiographic parameters

Echocardiographic assessment was done Pre-procedural, Post-implantation at 48 hours and at follow-up of 6 months in all patients. It is a good bedside screening tool for assessment of septal thickness, significant scar, LV dimensions, volumes and functions. We recommend echocardiographic assessment for all patients undergoing physiological pacing to evaluate for Tricuspid regurgitation, septal thickness and LV functions. Mean mid septal wall thickness was 10.45± 1.04 mm in our study population. No patients were excluded post echocardiographic screening for septal wall thickness in our study population. Baseline mean EF% was 46.70 ±11.14 % with 20 patients (47.6%) haing ejection fraction of less than 50% pre-implantation. Mean EF% increased to 48.17±9.53%; t value-3.226;p value= 0.002 on follow-up of 6 months. This was majorly seen in patients with Baseline Ejection fraction of less than 35% (6 patients) with mean EF of 26.00 ± 6.17% vs 31.40 ±7.92 at 6 months follow-up with GDMT along with physiological pacing. There was also improvement NYHA functional class with 0 % rehospializaion in patients with heart failure requiring CRT. The length of the lead inside the septum as measured in parasternal short axis was 9.6 ± 1.04 mm. There was no worsening of tricuspid regurgitation post implant or at 6 months of follow-up. In an observational, prospective, single center study by **Mirolo et al** [57] including 134 patients of LBBAP concluded that narrow QRS achieved with physiological pacing preserves mechanical synchrony in patients and was associated with an improvement of asynchrony parameters, in patients with both right and LBBB. Our findings are in concordance with study by **Ponnusamy et al** [54] reporting lead depth in the septum of 9.62 mm and increase in LV ejection fraction from 44.96 to 53.3% after LBBP ($p < 0.0001$).

9. Complications

In review of 530 published cases of Left bundle branch pacing, Complications noted were lead dislodgments in 6 patients (1%)(1 intraoperative, 3 within 24 hours, 1 at 2 months, and 1 at 4 months) and septal perforations in 9 (1.7%) (8 intraoperative and 1 patient at 1 month).[58] No other major complications associated with perforation, including transient ischemic attack/stroke and pericardial effusion have been described. Lead-related complications, such as infection, sensing issues, and delayed threshold rise, have not been reported. Other potential complications, such as intramural hematoma, coronary artery injury, tricuspid regurgitation, risk of septal contractile stress fracture of the lead, and risk of lead extraction, need to be investigated in future clinical studies. Our Study reports one case of macro-lead dislodgement during procedure which took place while slitting of sheath due to hardware related complication and 2 cases of micro lead dislodgement which were identified within 48 hours. No other complications like lead perforation, pericardial effusion, and pocket system infection were noted during duration of our study.

LIMITATIONS

This study will be our centers first series representing retro- prospective observational evaluation of physiological pacing by operators experienced in conventional right ventricular pacing. Further refinement of implant techniques would allow for easier implantation and higher success rates with less procedural time. Randomized studies are necessary to confirm the potential benefits of this approach in patients requiring pacemakers and CRT. Our study population was limited due to cost-effectiveness, hesitancy of patients towards newer technique, unsurety of benefits and indication, lack of consent and major role of COVID-19 pandemic as well. Also, benefits of physiological pacing could not be well co-related with pacing burden in our study due to a short term follow-up. This study needs more patients with LV dysfunction to strengthen the existing data for benefits of physiological pacing. We also could not measure procedural time and fluoroscopic time in our study. Future prospective studies and randomized studies with larger sample size, longer follow-ups and high pacing burdens are needed for better understanding and co-relation of physiological pacing.

Future perspective

Physiological pacing has been a rapidly progressing area in the field of cardiac resynchronisation therapy (CRT). Various large scale randomized clinical trials are still ongoing to evaluate long term benefits left bundle branch pacing over BiV-CRT. Future research on stylet driven leads for better manipulation and implantation, less procedural time and better capture is needed. Few cases on Leadless left bundle branch area pacing in cardiac resynchronization therapy have been published but needs further research for safety and feasibility.

SUMMARY AND CONCLUSION

SUMMARY

We conducted a retro-prospective study with an aim to study the feasibility of physiological pacing and its short term outcomes on electrophysiological, clinical and echocardiographic features.

- The study included 42 patients with a mean age of 62.7 ±8.3 years. There was a male predominance, with males accounting for 85% of the patients.
- The most common co-existing morbidities among the patients were hypertension (35.7%), diabetes mellitus (26.2%), coronary artery disease (26.2%), dilated cardiomyopathy (11.9%), and hypothyroidism (19%).
- The pacing indications amongst our study population was complete heart block (60%), sick sinus syndrome (10%), and cardiac resynchronization (10%).
- Physiological pacing was successful with implant success rate of 95.2% in our study which has been comparable with other prospective studies.
- There was a significant reduction in QRS duration after physiological pacing, which remained stable at 6 months of follow-up (133.1 ±13.48 msecs vs 111.8±14.53 msecs vs 115.2±10.86 msesc)
- Physiological pacing can be achieved at low pacing thresholds. We report similar low thresholds in our study remained near constant on short term follow-up(0.66±0.18 V vs. 0.67 ± 0.17 V, p=0.032) Which is well co-related to reduce risk of HF.
- Left ventricular activation time (LVAT) was within the range in our study, suggestive of left bundle branch pacing.(72.7±12.1 msecs).
- In our study lead impedance decreased during follow-up, indicating improved lead-to-tissue contact (738.1±113.3 Ω to 608.9±52.7 Ω; t=

6.795;p value=0.001). However there were no cases of impedance drop below 500 Ω with high pacing threshold need.

- In this study high R-wave amplitude were found which remained consistent, indicating optimal lead placement and timing of the pacing signal (10.1±2.0mV vs 10.1 ±1.4mV; t value 0.036;p value=0.971).
- We observed that patients with heart failure with reduced ejection fraction requiring CRT (N=4) benefited the most in clinical and echo cardiographic features with improved NYHA functional class and ejection fraction.
- There was no increase in functional class or clinical deterioration amongst our study population at implantation and on follow-up in our study.
- We report fewer complications in our study with no pacing system infections, lead fracture, lead displacement on follow-up. Micro lead dislodgement was noted in 2 patients and macro lead dislodgement while slitting of sheath was noted in 1 patient.

Overall, the study demonstrated successful physiological pacing with positive short-term clinical outcomes, including improved QRS duration, low pacing thresholds, appropriate LVAT, improved impedance, and consistent R-wave amplitude. Further research with a larger sample size is ongoing to gather more data and validate these findings.

CONCLUSION

We conclude that physiological pacing is achievable with high success rates and offers several advantages including a lower pacing threshold, narrower QRS duration, higher sensed R-wave amplitude parameters which remain stable during follow-up with increased safety. These lower thresholds and higher sensed R wave can further prevent early battery depletion. Due to capture and stimulation of naturally existing conduction system this technique also provides a synchronous ventricular activation

which can potentially prevent new onset heart failure due to PICM and AF. This additional benefit of preserving and even potentially enhancing left ventricular systolic functions has led to its use as a treatment option for cardiac resynchronization therapy as well. While long-term data still lacks, these benefits will presumably endure, making physiological pacing a novel technique which can be highly recommended and incorporated in future guidelines. We also conclude that physiological pacing, in addition to stable pacing parameters, has also demonstrated clinical, electrophysiological, and echocardiographic benefits in terms of short-term outcomes.

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S.No.	NAME	MRD	AGE	GENDER	COMPLAINT	FUNCTIONAL CLASS AT BASELINE	FUNCTIONAL CLASS AT 6months	Co-morbidities						ECG BEFORE PACING							
								CAD	HTN	DCMP	DM	VHD	HYPOTHYROIDISM	Minimum HR	RHYTHM	QRSd (in msecs)	LBBB	LAFB	LPFB	RBBB	AF
1	AC	1145678	72	1	3	1	1	0	1	0	1	0	0	35	3	145	0	0	0	0	0
2	VKA	1065119	60	1	1	2	2	0	1	0	0	0	0	44	2	134	0	0	0	1	0
3	MY	1070648	60	1	1	2	1	1	0	0	0	0	0	31	3	140	1	0	1	0	0
4	GS	578057	73	1	1	3	2	1	1	0	1	0	1	52	3	160	1	0	0	0	0
5	KS	1213216	62	1	1	1	1	0	1	0	0	0	0	60	3	165	1	0	0	0	0
6	PS	1036764	74	1	1	3	2	1	0	0	0	0	1	54	2	145	0	1	0	1	0
7	RA	333591	58	1	1	3	2	0	0	0	0	0	0	45	3	140	1	0	0	0	0
8	SS	96034	46	1	1	1	1	0	1	0	0	0	0	56	3	130	0	1	0	1	1
9	SK	1036101	57	1	1	1	1	0	0	0	1	0	0	60	2	162	0	1	0	0	0
10	K	1167566	51	1	2	1	1	1	1	0	1	0	0	36	3	130	0	0	0	1	0
11	KJ	333964	57	1	1	3	2	1	1	0	0	0	0	40	3	150	1	0	0	0	0
12	SKD	1296503	50	1	1	3	3	0	0	0	0	0	1	32	1	120	0	0	0	0	0
13	PS	1289101	63	1	1	3	2	0	1	0	0	0	0	40	2	144	1	0	0	0	0
14	BK	545858	56	1	1	3	2	0	0	0	0	0	0	54	2	130	0	0	0	1	0
15	MLK	129957	74	1	2	4	3	1	1	0	0	0	0	54	3	135	0	1	0	0	0
16	L	1246204	60	1	1	3	2	0	0	0	0	0	1	60	3	118	0	0	1	1	0
17	NA	203015	85	1	1	3	2	1	0	0	1	0	0	80	4	160	1	0	0	0	0
18	SK	1341532	62	1	1	1	1	1	0	0	1	0	0	40	3	130	0	0	0	1	0
19	SR	1340780	65	1	1	3	3	0	0	0	0	0	1	36	3	138	0	0	0	0	0
20	RR	1245309	61	2	1	3	3	0	0	0	0	0	0	32	1	130	0	0	0	0	1
21	PS	1332153	50	1	1	3	3	0	0	0	0	0	0	60	1	115	0	0	0	0	1
22	N	1319131	51	2	3	4	3	0	0	1	0	0	1	60	4	144	1	0	0	0	0
23	SS	207716	67	1	3	4	3	1	1	0	1	0	0	40	4	130	1	0	0	0	1
24	AK	1313109	60	1	1	3	3	0	0	0	0	0	0	44	3	130	0	0	0	0	0
25	HS	1315482	67	1	1	2	2	1	1	0	0	0	0	60	3	130	0	0	0	0	1
26	BG	1341527	65	1	1	3	2	0	1	0	1	0	0	48	3	140	0	0	0	0	0
27	AS	1320698	65	1	1	3	3	0	0	0	1	0	0	54	2	135	1	0	0	0	0
28	AN	116534	75	1	1	4	3	0	0	1	0	0	0	36	3	120	0	0	0	0	0
29	HK	1338603	65	2	1	3	3	0	0	0	0	0	0	45	3	120	0	0	0	0	0
30	SK	764342	59	1	3	4	3	0	0	1	0	0	0	70	4	130	1	0	0	0	0
31	TR	754517	70	1	1	4	3	0	0	0	0	0	0	28	3	130	0	0	0	1	1
32	KK	1347006	70	2	1	2	2	0	0	0	0	0	1	35	3	110	0	0	0	0	0
33	LRM	1381444	72	1	1	3	2	1	1	0	1	0	0	40	3	116	0	0	0	0	0
34	IS	1351601	76	1	1	2	2	0	0	0	1	0	0	38	2	118	0	0	0	0	0
35	KS	1369080	55	1	1	1	1	0	0	0	0	0	0	56	2	120	0	0	0	0	0
36	GK	1188655	57	2	1	1	1	0	0	0	0	0	0	40	1	120	0	0	0	0	0
37	GDS	1343763	67	1	1	1	1	0	0	0	0	0	0	48	3	118	0	0	0	0	0
38	RK	36782	53	1	1	3	3	0	0	1	0	0	0	42	3	130	1	0	0	0	0
39	AK	1164567	68	2	1	2	2	0	0	0	0	0	1	38	3	140	1	0	0	0	0
40	P	103654	57	1	1	2	2	0	0	1	0	0	0	42	3	142	1	0	0	0	0
41	VG	867269	60	1	1	1	1	0	1	0	0	0	0	44	3	118	0	0	0	0	0
42	JK	407113	61	2	1	1	1	0	1	0	0	0	0	70	3	130	1	0	0	0	0

S.No.	NAME	MRD	PACING PARAMETERS AT IMPLANTATION										PACING I	
			LBB potential	Sti-LVAT at 5 V/0.4 ms,	Capture threshold, V/0.5 ms	Capture type	Paced QRSd, ms	Pacing impedance, Ω	R wave amplitude, mV	Anodal Capture threshold (in V)	Transition zone	Sti-LVAT at 5 V/0.4 ms,	Capture threshold, V/0.5 ms	Paced QRSd, ms
1	AC	1145678	1	65	0.8	1	118	780	10	2	3	60	0.8	120
2	VKA	1065119	1	65	0.5	1	102	680	12	1	2	65	0.6	102
3	MY	1070648	1	65	0.6	1	100	740	9	2.2	2	70	0.6	110
4	GS	578057	0	65	0.6	1	118	580	3.5	2	3	56	0.6	122
5	KS	1213216	0	67	0.5	2	116	720	4	1	3	70	0.5	122
6	PS	1036764	1	70	0.6	1	116	800	12	1.6	3	64	0.6	120
7	RA	333591	1	88	0.8	1	120	650	8.5	1.6	3	90	0.8	122
8	SS	96034	1	75	0.6	1	115	850	11	1.8	4	75	0.6	115
9	SK	1036101	1	70	0.7	1	118	700	12.5	1	3	70	0.7	120
10	K	1167566	0	65	0.5	3	98	600	10	1.4	3	65	0.5	110
11	KJ	333964	1	65	0.6	1	116	650	10.5	2	4	65	0.6	118
12	SKD	1296503	1	70	0.4	1	118	800	12	1	2	65	0.4	120
13	PS	1289101	0	60	0.6	3	118	750	11	1.2	4	65	0.6	120
14	BK	545858	1	85	0.4	1	125	650	10	2	3	85	0.5	130
15	MLK	129957	0	75	0.5	2	116	600	8	1	3	75	0.5	120
16	L	1246204	1	60	0.6	1	130	700	9	1.2	2	60	0.6	130
17	NA	203015	0	80	1	2	120	900	9	1	3	95	1	116
18	SK	1341532	1	80	0.5	2	125	800	8.5	2	4	95	0.5	125
19	SR	1340780	1	73	0.6	1	92	900	12	2	3	75	0.6	100
20	RR	1245309	0	76	0.8	1	112	672	12	2	3	80	0.8	112
21	PS	1332153	1	82	0.7	3	120	580	8	1	3	82	0.7	100
22	N	1319131	1	66	0.6	1	120	740	12	2	2	65	0.6	120
23	SS	207716	1	71	0.6	1	120	690	11	1	2	71	0.6	120
24	AK	1313109	1	81	0.6	1	112	750	12	1.6	4	81	0.6	112
25	HS	1315482	0	88	0.8	3	110	800	12	1.6	2	88	0.8	110
26	BG	1341527	1	67	1	1	118	960	10	1	3	70	1	118
27	AS	1320698	1	81	0.8	1	120	800	9.5	1.2	3	80	0.8	120
28	AN	116534	1	66	1	2	110	700	8	1.5	2	66	1	110
29	HK	1338603	0	90	0.6	1	116	740	7	1.2	3	90	0.6	116
30	SK	764342	1	76	0.6	1	110	600	12	1	3	80	0.6	110
31	TR	754517	0	76	0.7	1	120	580	10	2	3	76	0.8	120
32	KK	1347006	1	69	0.5	3	90	900	12	1	2	70	0.5	100
33	LRM	1381444	1	70	0.8	1	110	842	10	2.2	2	72	0.8	110
34	IS	1351601	1	76	0.4	1	100	670	11	1.2	3	76	0.6	106
35	KS	1369080	0	64	0.6	1	98	760	8	1.6	2	64	0.6	80
36	GK	1188655	0	62	1	3	100	700	12	1	2	60	1	96
37	GDS	1343763	0	64	1.1	2	116	560	12	1.8	3	70	1.1	118
38	RK	36782	0	70	0.8	1	100	650	9	1.2	2	72	0.8	106
39	AK	1164567	0	92	0.6	2	130	1020	10	1.8	4	84	0.6	140
40	P	103654	0	88	0.4	2	136	980	12	1.5	4	90	0.4	136
41	VG	867269	0	68	0.6	1	118	720	12	2.2	3	68	0.6	120
42	JK	407113	0	70	0.7	1	118	740	10	1.8	3	70	0.8	118

S.No.	NAME	MRD	PARAMETERS AT 6 MONTHS			PROCEDURAL COMPLICATIONS							
			Pacing impedance, Ω	R wave amplitude, mV	Transition zone	Macro Lead dislodgement,	Micro Lead dislodgement	Lead perforation	Transient RBB injury	Persistent RBB injury	Pericardial effusion	Pacing system infection	Pocket hematoma
1	AC	1145678	560	12	3	0	0	0	0	0	0	0	0
2	VKA	1065119	600	10	2	0	0	0	0	0	0	0	0
3	MY	1070648	650	10	2	0	0	0	0	0	0	0	0
4	GS	578057	600	8	3	0	0	0	0	0	0	0	0
5	KS	1213216	540	8	3	0	0	0	0	0	0	0	0
6	PS	1036764	640	8	3	0	0	0	0	0	0	0	0
7	RA	333591	600	9	3	0	0	0	0	0	0	0	0
8	SS	96034	540	10	4	0	1	0	0	0	0	0	0
9	SK	1036101	500	12	3	0	0	0	0	0	0	0	0
10	K	1167566	650	11	3	0	0	0	0	0	0	0	0
11	KJ	333964	650	12	4	0	0	0	0	0	0	0	0
12	SKD	1296503	600	10	2	0	0	1	0	0	0	0	0
13	PS	1289101	640	10	4	1	0	1	0	0	0	0	0
14	BK	545858	650	8	3	0	0	0	0	0	0	0	0
15	MLK	129957	642	9	3	0	0	0	0	0	0	0	0
16	L	1246204	645	9	2	0	1	0	0	0	0	0	0
17	NA	203015	640	10	3	0	0	0	1	0	0	0	0
18	SK	1341532	650	9	4	0	0	0	0	0	0	0	0
19	SR	1340780	600	10	3	1	0	0	0	0	0	0	0
20	RR	1245309	540	12	3	0	0	0	0	0	0	0	0
21	PS	1332153	650	10	3	0	0	0	0	0	0	0	0
22	N	1319131	540	8	2	0	0	0	0	0	0	0	0
23	SS	207716	580	10	2	0	0	0	0	0	0	0	0
24	AK	1313109	500	10	4	0	0	0	0	0	0	0	0
25	HS	1315482	600	12	2	0	0	0	0	0	0	0	0
26	BG	1341527	640	13	3	0	0	0	0	0	0	0	0
27	AS	1320698	540	9.5	3	0	0	0	0	0	0	0	0
28	AN	116534	540	9	2	0	0	0	0	0	0	0	0
29	HK	1338603	600	10	3	0	0	0	0	0	0	0	0
30	SK	764342	560	9	3	0	0	0	0	0	0	0	0
31	TR	754517	600	8	3	0	0	0	0	0	0	0	0
32	KK	1347006	650	10	2	0	0	0	0	0	0	0	0
33	LRM	1381444	600	10	2	0	0	0	0	0	0	0	0
34	IS	1351601	650	10	3	0	0	0	0	0	0	0	0
35	KS	1369080	580	12	2	0	0	0	0	0	0	0	0
36	GK	1188655	650	10	2	0	0	0	0	0	0	0	0
37	GDS	1343763	620	10	3	0	0	0	0	0	0	0	0
38	RK	36782	680	9	2	0	0	0	1	0	0	0	0
39	AK	1164567	720	12	4	0	0	0	0	0	0	0	0
40	P	103654	560	14	4	0	0	0	0	0	0	0	0
41	VG	867269	680	10	3	0	0	0	0	0	0	0	0
42	JK	407113	700	12	3	0	0	0	0	0	0	0	0

S.No.	NAME	MRD			COMPLICATIONS AT 6 MONTHS			ECHOCARDIOG											
			Pneumothorax/ hemothorax	Pacing threshold > 2.0 V/0.4 ms	Lead dislodgement,	Lead perforation	Pacing system infection	LA	RA	RVID	IVST D	IVST S	LVID D	LVID S	LVPW D	LVPW S	MR (mild/mod/severe)	E/A	AR (mild/mod/severe)
1	AC	1145678	0	0	0	0	0	36	28	23	7	8	52	48	7	8	0	0.8	0
2	VKA	1065119	0	0	0	0	0	35	26	25	8	9	50	46	8	9	0	0.8	0
3	MY	1070648	0	0	0	0	0	37	29	25	8	7	47	37	6	8	0	1	0
4	GS	578057	0	0	0	0	0	34	30	29	7	7	56	52	8	9	1	1.5	0
5	KS	1213216	0	0	0	0	0	31	31	26	7	9	43	37	8	9	0	1.2	0
6	PS	1036764	0	0	0	0	0	35	33	28	8	9	42	32	8	9	0	1.1	0
7	RA	333591	0	0	0	0	0	48	32	36	7	8	54	50	7	8	1	1.8	0
8	SS	96034	0	0	0	0	0	32	24	27	8	7	58	30	7	8	0	1	0
9	SK	1036101	0	0	0	0	0	36	24	23	9	7	57	32	7	7	0	1	0
10	K	1167566	0	0	0	0	0	32	31	30	7	6	53	43	6	7	0	0.6	0
11	KJ	333964	0	0	0	0	0	30	22	28	6	9	53	28	8	7	0	0.8	0
12	SKD	1296503	0	0	0	0	0	30	33	23	8	8	42	28	7	6	2	0.6	0
13	PS	1289101	0	0	0	0	0	37	33	29	8	6	53	40	9	9	0	1.2	0
14	BK	545858	0	0	0	0	0	29	25	29	6	6	56	36	6	8	0	0.9	0
15	MLK	129957	0	0	0	0	0	34	28	27	7	7	54	28	6	9	0	1	0
16	L	1246204	0	0	0	0	0	39	33	25	7	9	54	33	6	9	0	0.8	0
17	NA	203015	0	0	0	0	0	44	46	26	7	8	46	31	6	8	0	1	0
18	SK	1341532	0	0	0	0	0	38	27	28	6	6	52	43	6	7	0	1.2	0
19	SR	1340780	0	0	0	0	0	32	26	27	9	8	53	39	7	8	0	1	0
20	RR	1245309	0	0	0	0	0	30	31	30	8	8	56	30	6	8	0	0.6	0
21	PS	1332153	0	0	0	0	0	36	30	30	8	6	55	38	6	6	0	0.8	0
22	N	1319131	0	0	0	0	0	36	30	24	7	6	58	31	7	7	0	1	0
23	SS	207716	0	0	0	0	0	48	46	30	7	8	58	52	6	7	2	1	1
24	AK	1313109	0	0	0	0	0	31	22	24	7	6	44	27	7	9	0	1	0
25	HS	1315482	0	0	0	0	0	29	27	25	6	7	51	33	7	8	0	1.2	0
26	BG	1341527	0	0	0	0	0	40	30	25	6	8	52	35	6	7	0	0.8	0
27	AS	1320698	0	0	0	0	0	35	29	29	8	8	44	42	6	7	0	1	0
28	AN	116534	0	0	0	0	0	40	24	31	7	6	47	36	8	8	0	0.8	0
29	HK	1338603	0	0	0	0	0	38	27	31	7	8	42	34	6	8	0	1	0
30	SK	764342	0	0	0	0	0	40	40	30	7	8	56	50	8	9	2	0.6	1
31	TR	754517	0	0	0	0	0	38	22	25	8	8	55	44	6	9	0	1	0
32	KK	1347006	0	0	0	0	0	37	26	30	6	8	48	41	7	6	0	1	0
33	LRM	1381444	0	0	0	0	0	36	34	28	7	8	42	38	7	8	0	0.9	0
34	IS	1351601	0	0	0	0	0	29	25	29	6	6	56	36	6	8	0	0.9	0
35	KS	1369080	0	0	0	0	0	36	28	23	7	8	52	48	7	8	0	0.8	0
36	GK	1188655	0	0	0	0	0	35	26	25	8	9	50	46	8	9	0	0.8	0
37	GDS	1343763	0	0	0	0	0	37	29	25	8	7	47	37	6	8	0	1	0
38	RK	36782	0	0	0	0	0	36	30	30	8	6	55	38	6	6	0	0.8	0
39	AK	1164567	0	1	0	0	0	48	32	36	7	8	54	50	7	8	1	1.8	0
40	P	103654	0	1	0	0	0	40	23	25	9	6	50	48	9	9	0	0.9	0
41	VG	867269	0	0	0	0	0	40	30	25	6	8	52	35	6	7	0	0.8	0
42	JK	407113	0	0	0	0	0	38	27	31	7	8	42	34	6	8	0	1	0

S.No.	NAME	MRD	RAPHY AT BASELINE																
			TR (mild/mod/severe)	PR (mild/mod/severe)	Pericardial effusion	SPWMD (M Mode) msecs	LVDV (in ml)	LVSV (in ml)	SV (in ml)	EF%	LA	RA	RVID	IVST D	IVST S	LVID D	LVID S	LVPW D	LVPW S
1	AC	1145678	1	0	0	63	128	60	68	53.13	36	28	23	7	8	52	48	7	8
2	VKA	1065119	0	0	0	70	126	75	51	51.00	35	26	25	8	9	50	46	8	9
3	MY	1070648	1	0	0	120	160	72	88	55.00	37	29	25	8	7	47	37	6	8
4	GS	578057	1	0	0	120	170	100	70	41.18	34	30	29	7	7	54	51	8	9
5	KS	1213216	0	0	0	160	130	61	69	53.08	31	31	26	7	9	43	37	8	9
6	PS	1036764	1	0	0	120	158	73	85	53.80	35	33	28	8	9	42	32	8	9
7	RA	333591	2	0	0	140	183	106	77	42.08	48	32	36	7	8	54	50	7	8
8	SS	96034	0	0	0	130	159	66	93	58.49	32	24	27	8	7	58	30	7	8
9	SK	1036101	0	0	0	100	131	74	57	43.51	34	22	23	8	9	46	39	9	8
10	K	1167566	1	0	0	98	119	64	55	46.22	40	30	31	8	7	57	32	9	7
11	KJ	333964	0	0	0	100	119	65	54	45.38	31	27	24	9	8	42	30	6	6
12	SKD	1296503	2	0	0	130	100	66	34	34.00	30	33	23	8	8	42	28	7	6
13	PS	1289101	1	0	0	120	147	73	74	50.34	39	26	25	7	6	43	28	6	7
14	BK	545858	0	0	0	130	159	66	93	58.49	40	23	25	9	6	50	25	9	9
15	MLK	129957	2	0	0	130	132	88	44	33.33	34	28	27	7	7	54	28	6	9
16	L	1246204	0	0	0	118	150	70	80	53.33	29	23	30	7	6	51	37	8	8
17	NA	203015	1	0	0	170	166	130	36	21.69	44	46	26	7	8	46	31	6	8
18	SK	1341532	0	0	0	98	141	67	74	52.48	29	25	26	8	6	45	34	7	6
19	SR	1340780	0	0	0	150	136	65	71	52.21	31	25	25	7	7	54	41	9	7
20	RR	1245309	0	0	0	115	121	69	52	42.98	38	29	27	8	9	45	39	9	6
21	PS	1332153	1	0	0	145	160	100	60	37.50	36	30	30	8	6	53	36	6	6
22	N	1319131	2	0	0	186	170	130	40	23.53	36	30	24	7	6	56	30	7	7
23	SS	207716	3	1	0	180	220	180	40	18.18	48	46	30	7	8	58	52	6	7
24	AK	1313109	0	0	0	88	153	68	85	55.56	33	33	27	9	8	55	30	8	6
25	HS	1315482	0	0	0	100	139	72	67	48.20	30	23	26	7	9	54	31	7	8
26	BG	1341527	0	0	0	78	133	59	74	55.64	30	27	28	7	6	45	30	9	9
27	AS	1320698	0	0	0	85	147	73	74	50.34	32	31	25	8	9	57	37	6	8
28	AN	116534	0	0	0	90	129	69	60	46.51	39	23	25	6	8	50	31	9	7
29	HK	1338603	0	0	0	120	147	61	86	58.50	32	23	23	8	8	44	39	6	6
30	SK	764342	2	0	0	160	200	160	40	20.00	40	40	30	7	8	54	49	8	9
31	TR	754517	0	0	0	120	145	64	81	55.86	34	33	27	8	9	47	42	9	8
32	KK	1347006	0	0	0	112	143	65	78	54.55	37	30	30	9	7	45	32	8	8
33	LRM	1381444	0	0	0	100	160	80	80	50.00	36	34	28	7	8	42	38	7	8
34	IS	1351601	0	0	0	130	159	66	93	58.49	29	25	29	6	6	56	36	6	8
35	KS	1369080	1	0	0	63	128	60	68	53.13	36	28	23	7	8	52	48	7	8
36	GK	1188655	0	0	0	70	126	75	51	51.00	35	26	25	8	9	50	46	8	9
37	GDS	1343763	1	0	0	120	160	72	88	55.00	37	29	25	8	7	47	37	6	8
38	RK	36782	1	0	0	145	160	110	50	31.25	36	30	30	8	6	55	46	6	6
39	AK	1164567	2	0	0	140	180	100	80	44.44	48	32	36	7	8	54	50	7	8
40	P	103654	0	0	0	130	159	130	60	37.74	40	23	25	9	6	50	25	9	9
41	VG	867269	0	0	0	78	133	59	74	55.64	30	27	28	7	6	45	30	9	9
42	JK	407113	0	0	0	120	147	61	86	58.50	32	23	23	8	8	44	39	6	6

S.No.	NAME	MRD	ECHOCARDIOGRAPHY AT 48 Hours Post-Implantation																		
			MR (mild/mod/severe)	E/A	AR (mild/mod/severe)	TR (mild/mod/severe)	PR (mild/mod/severe)	Pericardial effusion	SPWMD (M Mode)	LVDV	LVSV	SV	EF%	LA	RA	RVID	IVST D	IVST S	LVID D	LVID S	LVPW D
1	AC	1145678	0	0.8	0	1	0	0	63	128	60	68	53.13	36	28	23	7	8	52	48	7
2	VKA	1065119	0	0.8	0	0	0	0	70	126	75	51	51.00	35	26	25	8	9	50	46	8
3	MY	1070648	0	1	0	1	0	0	120	160	72	88	55.00	37	29	25	8	7	47	37	6
4	GS	578057	1	1	0	1	0	0	120	170	90	80	47.06	34	30	29	7	7	54	52	8
5	KS	1213216	0	1.2	0	0	0	0	160	130	61	69	53.08	31	31	26	7	9	43	37	8
6	PS	1036764	0	1.1	0	1	0	0	120	152	70	82	53.95	35	33	28	8	9	42	32	8
7	RA	333591	1	1.8	0	2	0	0	140	180	100	80	44.44	48	32	36	7	8	52	48	7
8	SS	96034	0	1	0	0	0	0	130	159	66	93	58.49	32	24	27	8	7	58	30	7
9	SK	1036101	0	1	0	0	0	1	100	131	74	57	43.51	38	30	29	8	6	53	41	9
10	K	1167566	0	0.6	0	0	0	0	98	119	64	55	46.22	32	26	23	6	7	46	31	8
11	KJ	333964	0	0.8	0	0	0	0	100	119	65	54	45.38	34	22	31	6	7	55	28	6
12	SKD	1296503	2	1	0	2	0	0	130	98	60	38	38.78	30	33	23	8	8	42	28	7
13	PS	1289101	0	1.2	0	0	0	0	120	147	73	74	50.34	37	25	29	8	6	51	33	8
14	BK	545858	0	0.9	0	0	0	0	130	159	66	93	58.49	30	25	23	8	9	45	38	6
15	MLK	129957	0	1	0	2	0	0	130	132	88	44	33.33	34	28	27	7	7	54	28	6
16	L	1246204	0	0.8	0	0	0	0	118	150	70	80	53.33	29	32	26	9	8	52	41	7
17	NA	203015	0	1	0	1	0	1	140	154	120	34	22.08	44	46	26	7	8	46	31	6
18	SK	1341532	0	1.2	0	0	0	0	98	141	67	74	52.48	37	33	26	8	6	50	38	9
19	SR	1340780	0	1	0	0	0	0	150	136	65	71	52.21	40	22	23	9	6	58	36	6
20	RR	1245309	0	0.6	0	0	0	0	115	121	69	52	42.98	31	29	28	9	8	49	31	8
21	PS	1332153	0	0.8	0	1	0	0	145	160	100	60	37.50	36	30	30	8	6	53	36	6
22	N	1319131	0	1	0	2	0	0	160	150	110	40	26.67	36	30	24	7	6	56	30	7
23	SS	207716	2	1	1	3	1	0	140	200	160	40	20.00	48	46	30	7	8	58	52	6
24	AK	1313109	0	1	0	0	0	0	88	153	68	85	55.56	29	24	29	9	6	51	38	9
25	HS	1315482	0	1.2	0	0	0	0	100	139	72	67	48.20	34	30	31	9	7	43	30	6
26	BG	1341527	0	1	0	0	0	0	78	133	59	74	55.64	33	24	27	8	6	45	37	8
27	AS	1320698	0	0.9	0	0	0	1	85	147	73	74	50.34	34	29	26	7	8	42	31	8
28	AN	116534	0	1	0	0	0	0	90	129	69	60	46.51	34	31	28	9	7	47	35	6
29	HK	1338603	0	0.9	0	0	0	0	120	147	61	86	58.50	37	32	25	7	8	55	27	6
30	SK	764342	2	0.4	1	2	0	0	160	180	140	40	22.22	40	40	30	7	8	54	49	8
31	TR	754517	0	1	0	0	0	0	120	145	64	81	55.86	35	24	23	6	6	43	36	7
32	KK	1347006	0	1	0	0	0	0	112	143	65	78	54.55	35	29	26	8	6	44	36	8
33	LRM	1381444	0	0.9	0	0	0	0	100	160	80	80	50.00	36	34	28	7	8	42	38	7
34	IS	1351601	0	0.8	0	0	0	0	100	159	66	93	58.49	29	25	29	6	6	56	36	6
35	KS	1369080	0	0.8	0	1	0	0	63	128	60	68	53.13	36	28	23	7	8	52	48	7
36	GK	1188655	0	0.8	0	0	0	0	70	126	75	51	51.00	35	26	25	8	9	50	46	8
37	GDS	1343763	0	1	0	1	0	0	120	160	72	88	55.00	37	29	25	8	7	47	37	6
38	RK	36782	0	0.8	0	1	0	0	145	145	90	55	37.93	36	30	30	8	6	55	38	6
39	AK	1164567	1	1.8	0	2	0	0	140	180	100	80	44.44	48	32	36	7	8	54	50	7
40	P	103654	0	0.9	0	0	0	0	130	159	150	62	38.99	40	23	25	9	6	50	25	9
41	VG	867269	0	1	0	0	0	0	78	133	59	74	55.64	33	24	27	8	6	45	37	8
42	JK	407113	0	0.9	0	0	0	0	120	147	61	86	58.50	37	32	25	7	8	55	27	6

S.No.	NAME	MRD	ECHOCARDIOGRAPHY AT 6months Post-Implantation												
			LVPW S	MR (mild/mod/severe)	E/A	AR (mild/mod/severe)	TR (mild/mod/severe)	PR (mild/mod/severe)	Pericardial effusion	SPWMD (M Mode)	LVDV	LVSV	SV	EF%
1	AC	1145678	8	0	0.8	0	1	0	0	63	128	60	68	53.13
2	VKA	1065119	9	0	0.8	0	0	0	0	70	126	75	51	51.00
3	MY	1070648	8	0	1	0	1	0	0	120	160	72	88	55.00
4	GS	578057	9	1	1.2	0	1	0	0	120	160	80	80	50.00
5	KS	1213216	9	0	1.2	0	0	0	0	160	110	52	58	52.73
6	PS	1036764	9	0	1.1	0	1	0	0	120	145	69	76	52.41
7	RA	333591	8	1	1.4	0	2	0	0	120	160	78	82	51.25
8	SS	96034	8	0	1	0	0	0	0	130	159	66	93	58.49
9	SK	1036101	7	0	1	0	0	0	0	130	130	71	59	45.38
10	K	1167566	7	0	0.6	0	0	0	0	100	120	64	56	46.67
11	KJ	333964	8	0	0.8	0	0	0	0	98	119	65	54	45.38
12	SKD	1296503	6	1	0.6	0	1	0	0	130	100	62	38	38.00
13	PS	1289101	6	0	1	0	0	0	0	120	147	73	74	50.34
14	BK	545858	7	0	0.6	0	0	0	0	130	159	66	93	58.49
15	MLK	129957	9	0	0.8	0	2	0	0	130	132	80	52	39.39
16	L	1246204	8	0	0.9	0	0	0	0	118	150	70	80	53.33
17	NA	203015	8	0	0.8	0	1	0	0	140	148	110	38	25.68
18	SK	1341532	8	0	1.2	0	0	0	0	98	141	67	74	52.48
19	SR	1340780	9	0	1	0	0	0	0	150	136	65	71	52.21
20	RR	1245309	6	0	0.6	0	0	0	0	115	121	69	52	42.98
21	PS	1332153	6	0	0.8	0	1	0	0	145	160	100	60	37.50
22	N	1319131	7	0	1	0	1	0	0	160	138	100	38	27.54
23	SS	207716	7	2	1	1	3	1	0	140	188	150	38	20.21
24	AK	1313109	6	0	1	0	0	0	0	88	150	65	85	56.67
25	HS	1315482	7	0	0.8	0	0	0	0	100	139	72	67	48.20
26	BG	1341527	9	0	0.6	0	0	0	0	78	133	59	74	55.64
27	AS	1320698	6	0	0.9	0	0	0	0	85	147	73	74	50.34
28	AN	116534	9	0	1	0	0	0	0	90	129	69	60	46.51
29	HK	1338603	9	0	1	0	0	0	0	120	147	61	86	58.50
30	SK	764342	9	2	0.4	1	2	0	0	160	176	130	46	26.14
31	TR	754517	9	0	1.1	0	0	0	0	120	145	64	81	55.86
32	KK	1347006	7	0	1.2	0	0	0	0	112	143	65	78	54.55
33	LRM	1381444	8	0	0.9	0	0	0	0	100	160	80	80	50.00
34	IS	1351601	8	0	0.9	0	0	0	0	98	159	66	93	58.49
35	KS	1369080	8	0	0.8	0	1	0	0	63	128	60	68	53.13
36	GK	1188655	9	0	0.8	0	0	0	0	70	126	75	51	51.00
37	GDS	1343763	8	0	1	0	1	0	0	120	160	72	88	55.00
38	RK	36782	6	0	0.8	0	1	0	0	145	140	80	60	42.86
39	AK	1164567	8	1	1.8	0	2	0	0	140	180	100	80	44.44
40	P	103654	9	0	0.9	0	0	0	0	130	148	148	62	41.89
41	VG	867269	9	0	0.6	0	0	0	0	78	133	59	74	55.64
42	JK	407113	9	0	1	0	0	0	0	120	147	61	86	58.50

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The Principal,
DMC, Ludhiana.

Subject: **Approval of Plan of Thesis.**

This is to inform you that the Faculty of Medical Sciences in its meeting held on 29.10.2021 has approved the plan of thesis of **Bhavuk Jaiswal,** a student of your college for **DM Cardiology** along with the names of Supervisor/Co-Supervisor as under:-

Topic Plan of Thesis
A retro-prospective study of physiological pacing and its short term outcomes.

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The student has to submit the four copies of thesis (along with PDF format) , to the Controller of Examinations, BFUHS, Faridkot, at least six months before the commencement of theory examination, if he/she is otherwise eligible to take the examination. He /She must directed to attach a photocopy of this letter with the forwarding letter while submitting thesis to the University along with the letter of approval of University for change of supervisor/Co-Supervisor, change of topic,(if any).

Dr. S P Singh MS(Oph)
Controller of Examinations

Note :

155. If any discrepancy found regarding topic of thesis or Supervisor/Co-Supervisor, inform undersigned within one month after issue of this letter.

156. The student may submit the thesis as per the schedule already conveyed i.e for May/June examination 30th Nov of the preceding the year of examination and for Nov/Dec examinations 31st May of the year of examination.

A RETRO-PROSPECTIVE STUDY OF PHYSIOLOGICAL PACING AND ITS SHORT TERM OUTCOMES

THESIS PROPOSAL

FOR APPROVAL OF SUBJECT OF THESIS TO BE SUBMITTED

IN PARTIAL FULFILMENT OF THE REQUIREMENTS

FOR THE DEGREE OF

DOCTORATE OF MEDICINE

IN

CARDIOLOGY

OF THE

BABA FARID UNIVERSITY OF HEALTH SCIENCES
FARIDKOT

AUGUST, 2021

DR BHAVUK JAISWAL

DEPARTMENT OF CARDIOLOGY
DAYANAND MEDICAL COLLEGE & HOSPITAL
LUDHIANA

ABSTRACT OF PLAN OF THESIS

Title	A RETRO-PROSPECTIVE STUDY OF PHYSIOLOGICAL PACING AND ITS SHORT TERM OUTCOMES.
For the degree of	D.M Cardiology
Name of the candidate	Dr Bhavuk Jaiswal
Supervisor	Dr Naved Aslam, Professor, Department of Cardiology, DMCH, Ludhiana
Co-supervisor	Dr Shibba Takkar Chhabra, Professor, Department of Cardiology, DMCH, Ludhiana Dr Abhishek Goyal, Associate Professor, Department of Cardiology, DMCH, Ludhiana
Institution	Dayanand Medical College & Hospital, Ludhiana
University	Baba Farid University of Health Sciences, Faridkot

Introduction: Cardiac pacing is the only effective therapy for patients with symptomatic brady-arrhythmias. Physiological pacing activates the normal cardiac conduction in contrast to traditionally used right ventricle apical pacing causing mechanical and electrical dyssynchrony. His and Left bundle branch pacing modalities have emerged as an alternative method for delivering pacing to cardiac conduction system.

Aim of Study: To study effects of physiological pacing and its short term outcomes on clinical status, electrocardiogram, echocardiographic and lead parameters on 6 months of follow-up.

Materials & Methods: Patient meeting inclusion criteria's will be analyzed for NYHA functional class, electrocardiogram and echocardiographic parameters initially before pacemaker implantation with an initial attempt of physiological pacing of His bundle or Left Bundle branch following which lead parameters, electrocardiogram and echocardiographic parameters will be reassessed post implantation and after 6 months of follow-up. Data collected will be analyzed using appropriate statistical analysis.

Clinical Significance: Physiological pacing is a recent technique of pacing. This modality of pacing has been suggested as an effective alternative to overcome various limitations to provide low and stable pacing threshold, lead stability, and correction of distal conduction system disease. This has been a topic of interest for many interventional cardiologists and limited by scarcity of literature.

Keywords: His- bundle pacing, Left bundle branch pacing, Cardiac-Electrophysiology, Brady-arrhythmias, Physiological pacing

(Signature)	(Signature)	(Signature)	(Signature)	(Signature)
Candidate	Co-supervisor	Co-supervisor	Supervisor	Principal

CERTIFICATE OF FACILITIES AVAILABLE

This is to certify that the facilities for work on the subject of thesis titled **"A RETRO-PROSPECTIVE STUDY OF PHYSIOLOGICAL PACING AND ITS SHORT TERM OUTCOMES."** exist in the Department of Cardiology, DMC&H, and Ludhiana and will be provided to the candidate. We will see that the data being included in the thesis is genuine and is collected by the candidate himself under our supervision and guidance.

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APPROVAL PROFORMA
BY RESEARCH & ETHICAL COMMITTEE
DAYANAND MEDICAL COLLEGE & HOSPITAL, LUDHIANA

Name of candidate	Dr. Bhavuk Jaiswal
Department	Cardiology
Topic of Thesis	A RETRO-PROSPECTIVE STUDY OF PHYSIOLOGICAL PACING AND ITS SHORT TERM OUTCOMES
Likely date of appearing in PG examination	MAY-JUNE, 2023
Date of enrollment	26.12.2020
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Dr. Harpreet Kaur (Professor & Head, Pathology)	Mr. R K Sharma (Legal Expert)
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BABA FARID UNIVERSITY OF HEALTH SCIENCES, FARIDKOT

PROFORMA FOR REGISTRATION OF SUBJECT FOR DISSERTATION

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2	NAME OF THE INSTITUTE	DAYANAND MEDICAL COLLEGE AND HOSPITAL LUDHIANA
3	COURSE OF STUDY AND SUBJECT	DM CARDIOLOGY
4	DATE OF ADMISSION OF COURSE	26 December 2020
5	TITLE OF THE TOPIC	A Retro-Prospective Study of Physiological pacing and its short term outcomes.

6 BRIEF RESUME OF THE INTENDED WORK

6.1 NEED FOR THE STUDY

Cardiac Conduction disorders are a major health problem among cardiovascular related diseases, with increasing incidences, especially in elderly population due to age dependent, progressive, degenerative fibrosis. During normal aging, the number of pacemaker cells in the sinoatrial (SA) node declines significantly after age 60 years, with < 10% of the cells seen in young adults remaining by age 75. Till date, cardiac pacing has been the gold standard treatment of choice for any symptomatic bradyarrythmias due to sinus node dysfunction or Atrio-ventricular nodal diseases since the invention of cardiac pacing in the 1950s.The use of CIED has remarkably increased, all over the world, in the last decade. In India, Cardiac Conduction disorders constitutes as an important health problem as well. The Eucomed data on total number of CIED units sold in India in the year 2013 was 37,000 [1]. According to survey done by The Indian Society of Electrocardiology and Indian Heart Rhythm Society of cardiac implantable electronic device implantation in India revealed that Amongst the 2117 survey forms, Majority of 80% of the CIED implants in India were pacemakers for Bradycardia indications whereas 10% were ICD implants and 10% were CRT-P/CRT-D. The most common indication for Pacemaker implantation was complete atrio-ventricular block (76%) [1]. India has a higher percentage of complete AV block and relatively younger population, with most receiving a single chamber pacemaker [1]. The traditional right ventricular apical pacing (RVAP) has been widely used for more than half a century and has been very well-tolerated and effective in the past. However, the detrimental effects of Right ventricular apical pacing have been very well established due to electrical and mechanical dyssynchrony causing impaired myocardial perfusion,mitral and tricuspid regurgitation and an increased risk of atrial fibrillation, and systolic contractile dysfunction. Other ventricular pacing sites, such as the right ventricular septal (RVS) and right ventricular outflow tract (RVOT), have also been developed to minimize these adverse effects, however their long term outcomes have not

been demonstrated to be superior to RVAP [2,3]. Another pacing modality employed for treatment of HF is Cardiac resynchronization therapy via Bi-ventricular pacing, which demonstrated that CRT promotes left ventricular reverse remodeling, exercise tolerance, and reduces morbidity as well as mortality in patients with HFrEF. The benefits of BVP are well demonstrated but has been associated with significantly high non-response rate (30–40%) [4]. The Bi-ventricular pacing approach however beneficial is still non-physiological and requires two leads to activate the ventricular myocardium and not use the specialized cardiac conduction system. Therefore, the search and need for an ideal physiological pacing technique that directly activates conduction systems has become the focus of attention for years now. The specialized fibers of the His-Purkinje system are part of normal phyiological conduction of an impulse and essential for the maintenance of the coordinated, synchronous ventricular contraction via endocardial to epicardial and apical to basal electrical activation. Deshmukh et al.[5] were the first to demonstrate the feasibility of permanent His bundle pacing (HBP) in patients with AF and dilated cardiomyopathy following which multiple studies [6,7] have confirmed the clinical benefits of permanent His Bundle Pacing as a physiological site for pacing. Currently, HBS represents an alternative to conventional right or biventricular pacing in the following conditions: (1) high-degree atrioventricular (AV) block with expected ventricular pacing >20% of the time, (2) AV block 1st degree with long PQ (alone or in combination with intermittent 2nd to 3rd degree AV block or sick sinus syndrome), (3) AV node ablation due to refractory atrial fibrillation, and (4) upgrade in pacing-induced cardiomyopathy.[8]

HBP has been recommended as a rescue modality for failed BVP and even as a primary treatment for CRT[8].In recent years tools dedicated to His pacing have been developed, which have improved the ease with which His pacing can be delivered. His pacing is now technically feasible in most patients and has shown promising results in small, mainly non-randomised studies in various clinical situations.

There is currently limited published data available for His-Bundle pacing in any clinical setting. Pacing thresholds for His-Bundle pacing in bradycardia appear to be stable, there is limited long-term follow-up data. When His pacing is used to deliver ventricular resynchronisation in patients with bundle branch block, the pacing thresholds can be relatively high, though comparable to left ventricular pacing thresholds. This has further potential implications on battery longevity, even though pacing is only required via a single lead when compared to biventricular pacing. Success rates for His lead implantation have been as low as 60 % previously without dedicated tools and experience. However Success rates have improved with the development of dedicated tools but the range of tools currently available are still limited. Moreover as demonstrated by His Bundle Pacing vs. Coronary Sinus Pacing for Cardiac Resynchronization Therapy (His-SYNC) study, QRS duration (QRSd) could not be normalized in almost half of patients [9]. To address the above mentioned issues, researchers have recently developed the left bundle branch pacing (LBBP) therapy, as an emerging and a promising novel pacing modality for delivering physiological pacing and achieve electrical synchrony of the left ventricle. Compared to His Bundle pacing, LBBAP has benefits of large anatomic target site, technically less challenging procedure, easier lead fixation, shorter procedural and fluoroscopic times,higher success rates, ability to preserve or improve LV synchrony and, most importantly, stable lead parameters.[10]

Huang et al [11] in 2017 were first to report the technique to directly capture the left bundle branch (LBB) by deep septal pacing, which has the potential to overcome the limitations of HBP and showed benefits in patients with dilated cardiomyopathy. Following which few studies have reported benefits with this new technique of physiological pacing which included lead stability and better pacing parameters, longer battery life as compared to HBP, improvement in LV function, LV remodelling and resynchronization of ventricular contraction, narrower QRSd on follow ups, easier to perform than HBP, and even improvement in clinical outcomes.

Major complications related to left bundle branch pacing reported were tricuspid regurgitation, right bundle branch injury, lead dislodgement and septal perforation.[12]

These new novel modalities of physiological pacing technique of His-bundle and Left bundle branch area has been the topic of interest for many researchers and interventional cardiologists due to its advantages over traditional right ventricular pacing, being a recent technique it lacks enough real world data with selected study of populations and limited long term outcome studies. There are only few single Centre, follow up studies on physiological pacing of both His-Bundle and Left bundle branch area pacing comparing both methods and various other parameters with follow up.

6.2 REVIEW OF LITERATURE

Physiological pacing is a novel method of stimulating the normal cardiac conduction system for synchronous inter- and intra- ventricular activation. His bundle pacing in humans to stimulate the His-Purkinje system and produce normal physiological ventricular activation was first described in 1970 by Narula et al. However, the first report of permanent His bundle pacing was done by Deshmukh et al. in 2000[5]. Due to lack of dedicated tools for implantation, lower success rates and difficult technique initially hampered the enthusiasm; however, the development of specially designed sheaths and leads for delivering permanent His bundle pacing has led to a renewed interest.

The potential role of His pacing has been demonstrated in (1) high-degree atrioventricular (AV) block with expected ventricular pacing >20% of the time, (2) AV block 1st degree with long PQ (alone or in combination with intermittent 2nd to 3rd degree AV block or sick sinus syndrome), (3) AV node ablation due to refractory atrial fibrillation, (4) upgrade in pacing-induced cardiomyopathy (5)alternative to biventricular pacing in patients with heart failure and left bundle branch block (LBBB); and it may extend pacing therapy in heart failure to patients with narrow QRS and PR prolongation by providing AV synchrony without inducing ventricular dyssynchrony [13].

The bundle of His extends from the compact AV node to the membranous interventricular septum, and measures approximately 20 mm in length. The bundle is a cord-like structure made up of multiple strands, which, even before the branching, are predestined to become the right or left bundle branches. His bundle pacing can be achieved by placing the lead at the atrial portion against the septum.

The most commonly used lead for His bundle pacing is the 69 cm Select Secure™ 3830 (Medtronic). This is a non-stylet-driven active fixation lead. Importantly, the screw forms part of the tip electrode allowing penetration of the capsule of the bundle of His and, therefore, direct stimulation of the His bundle fibres. The lead can be delivered to the His bundle region using either the specially designed non-deflectable His delivery sheath (C315 43 cm; Medtronic) or a

deflectable sheath (C304 69 cm; Medtronic). Unlike traditional lead placement that primarily uses fluoroscopic guidance, His lead placement primarily uses electrical mapping. An electrogram from the lead tip is displayed using placement via either a lab electrophysiology system or a standard pacing system analyser.

To confirm successful His capture, a 12-lead ECG is used to assess the QRS morphology with pacing. Criteria used to establish whether His capture has occurred are well described. Recently-published data suggests thresholds of <2.5 at 1 ms should be achieved. An increase in pacing threshold is observed in ~10 % of patients, leading to shorter battery duration.[14] There is also a higher rate of lead revisions (6.7 %) due to loss of capture or increased threshold.[15]

His bundle capture may be either selective or non-selective. With selective capture, only the His bundle fibres are stimulated and, therefore, activation occurs entirely via the His-Purkinje system. With non-selective capture both the His bundle fibres and local myocardium are captured. During non-selective capture a pseudo delta wave on the surface ECG is formed from local myocardial capture.

Zanon et al. 2008 conducted a Non-randomised crossover study of 12 patients following 3 months of His pacing and 3 months of RVP. Intra-patient myocardial perfusion (myocardial perfusion score) during His pacing compared to RVP Myocardial perfusion score during His pacing was better than RVP.[16]

Catanzariti et al. in 2013 conducted a non-randomised crossover study of 26 patients to Measure echocardiographic dyssynchrony parameters during His pacing and RVP (intra-patient comparison) and showed Reduction of pacing-induced ventricular dyssynchrony with His pacing.[17]

Ajijola et al. 2017, Retrospective observational with a 76 % (16/21) successful His Pacing rate, with outomes measured for QRS duration, left ventricular ejection fraction, left ventricular dimensions and NYHA class showed Reduced QRS duration and improved left ventricular ejection fraction, reduced left ventricular dimensions and reduced NYHA class with His pacing [18].

Sharma et al. 2017 Retrospective observational study with purpose to report permanent HBP in patients undergoing pacemaker implantation after PV surgery showed a success rate of 90 % (95/106) also showed Improved left ventricular ejection fraction and NYHA, QRS duration shortening with His pacing. Thirty patients (47% men, age 74 ± 12 years, left ventricular ejection fraction 49% ± 11%) with AV conduction disease (100% patients; 14 with infranodal block; right bundle branch block 9, left bundle branch block 5, intraventricular conduction delay 1) underwent HBP. PVs included aortic valve replacement (AVR) in 8 patients (infranodal block 6 patients), tricuspid valve (TV) ring with mitral valve replacement or repair (MVR) in 10 patients (AV nodal block 9 patients), transcatheter aortic valve replacement (TAVR) in 4 patients (infranodal block 4 patients), and MVR alone in 6 patients. HBP was successful in 28 patients (93%) (selective HBP 50%). His bundle (HB) recruitment was unsuccessful in 2 patients with TAVR. AVR/TAVR and TV ring served as anatomic landmarks for localizing the HB. Successful sites of HBP were posterior and inferior to AVR/TAVR and distal and septal to the TV ring. Baseline QRSd improved from 124 ± 32 ms to 118 ± 20 ms (P = .39). HBP threshold at implant was 1.45 ± 1 V at 1 ms [19].

Recently, the resurgence of conduction system pacing (CSP) for patients with symptomatic bradycardia and heart failure has become the topic of interest. His-bundle pacing (HBP) is now an accepted alternative to more traditional ventricular pacing sites (right ventricular [RV] apex/outflow tract, coronary sinus).Although HBP is theoretically the ideal physiological pacing site, it has some inherent limitations. The implant technique requires greater expertise in targeting a small zone and can be challenging in patients with dilated hearts, resulting in long procedural and fluoroscopic times. The reported success rate for HBP varies from 56% to 95%, depending on the degree of conduction system disease present and the experience of the center [20–22].Successful HBP lead implantation is fraught with troubleshooting issues during follow-up.5 HBP leads typically have a low R-wave amplitude that may result in oversensing of atrial or His signals and

undersensing of ventricular signals. High HBP capture thresholds at implant and/or during late follow-up may result in premature battery depletion and repeated generator replacements and the associated risks. The unpredictable, delayed rise in HBP capture thresholds are a major concern, resulting in higher lead revision rates. A subset of patients may also lose His capture during followup, resulting in RV septal pacing.HBP leads are available. In the largest observational, 2-center study, 844 patients who received HBP leads had a mean pacing capture threshold of 1.6 V at implant and 2 V at median follow-up of 3 years.HBP was free of any complications in 91% of patients. However, a careful appraisal of the data highlights the concerns noted in about 35%–40% of the patients. Pacing thresholds were < 2.5 V at 1 ms in 28% of patients at median follow-up. Follow-up electrocardiography showed septal pacing in 9% of patients. Lead revision was required in 7.6% of patients. Median time for battery replacement was 5.8 years [23]. The quest for an optimal pacing site led to a novel CSP technique described by Huang et al in 2017,[11] where the pacing lead was implanted deep in the RV basal septum to capture the left bundle branch (LBB) area in a patient with heart failure and left bundle branch block (LBBB). LBBAP is rapidly emerging as an alternative for failed HBP cases or as a primary strategy for CSP. Both anatomy (narrow target for His bundle [HB] vs wide target for left bundle branch area [LBBA]) and histology (His encased in fibrous, electrically nonconducting tissue vs LBB embedded in myocardium) favor LBBA over HB for physiological pacing.

LBBAP is performed using a SelectSecure 3830 pacing lead (Medtronic, Minneapolis, MN), delivered via either the fixed-curve C315-HIS sheath or the new SelectSite C304HIS deflectable sheath (Medtronic). The 12-lead electrocardiographic recording and the intracardiac electrograms (EGMs) from the pacing lead are simultaneously displayed and continuously recorded on an electrophysiological recording system[23]

Deshmukh et al[5] showed 18 patients aged 69+/-10 years who had a history of chronic atrial fibrillation, dilated cardiomyopathy, and normal

activation (ie, QRS< or =120 ms) were screened for permanent DHBP using an electrophysiology catheter out of which 14 patients, His bundle could be reliably stimulated. Of these 14, permanent DHBP using a fixed screw-in lead was successful in 12 patients. Acute pacing thresholds were 2.4+/-1.0 V at a pulse duration of 0.5 ms. Lead complications included exit block requiring reoperative adjustment and gross lead dislodgment. Echocardiographic improvement in heart function was shown by reductions in the left ventricular end-diastolic dimension from 59+/-8 to 52+/-6 mm (P</=0.01) and in the end-systolic dimension from 51+/-10 to 43+/-8 mm (P<0.01), with an accompanying increase in fractional shortening from 14+/-7% to 20+/-10% (P=0.05). The left ventricular ejection fraction also improved from 20+/-9% to 31+/-11% (P<0. 01).

Huang et al (2021) [24] were able to conduct a large observational study suggesting LBBP is feasible with high successful rate of LBB capture [97.8% (618/632 patients)]with low LBB capture threshold at implant of 0.65±0.27 mV at 0.5 ms and 0.69±0.24 mV at 0.5 ms at 2-year follow-up. A significant decrease in QRS duration was observed in patients with left bundle branch block (167.22±18.99 versus 124.02±24.15 ms, P<0.001). Post-implantation left ventricular ejection fraction also improved in patients with QRS≥120 ms (48.82±17.78% versus 58.12±13.04%, P<0.001).

Vijayaraman et al. in 2019 [25] showed that LBBP was successful in 93 of 100 patients (93%). Pacing threshold at implant was 0.6± 0.4V @ 0.5ms pulse width and R waves were 10±6mV and remained stable at a median follow up of 3 months.

Li et al.(2019) [26] demonstrated the efficacy of LBBP in bypassing the level of block in patients with AV nodal disease successfully in 90% of patients (30 of 33patients) with a shorter paced QRSduration of 112.8± 10.9 s during the procedure and remained stable during follow-up along with improvement in LVfunction by strain imaging at 3-month follow-up.

Chen et al.(2019) [27] compared the ECG and pacing parameters between LBBP and RV pacing (RVP) in total of 40 patients which were

prospectively evaluated out of which 20 underwent RVP and 20 underwent LBBP. The paced QRS duration was significantly lower in LBBP group as compared to RVP group (111.85± 10.7ms vs 160± 15.04ms ; P< 0.001). Pacing thresholds were comparable and remained low and stable at 3-month follow- up. They were also able to demonstrate LBBP as a safe and effective strategy for patients in need of ventricular pacing.

LBBP has the potential to be an effective alternative to cardiac resynchronization therapy in patients with heart failure with LV dysfunction. Zhang et al. (2019) [28] enrolled 11 patients with heart failure with low ejection fraction and LBBB. LBBP significantly shortened QRS duration and LVAT. They also demonstrated resynchronization of ventricular contraction with LV reverse remodeling and significant improvement in clinical symptoms.

Hou et al. (2019) [29] demonstrated the mechanical synchrony of LV contraction after LB pacing and HBP using gated single-photon emission CT (SPECT) myocardial perfusion imaging and compared it with RV septal pacing and demonstrated that paced QRS duration in LBBP was significantly shorter than in the RV septal pacing group and wider than in the HBP group. LB pacing patients with LB potential had similar synchronized LV contraction as in the HBP group. LBBP achieved favourable cardiac electrical and LV mechanical synchrony.

Shunmuga et al (2020) [30] performed study to assess the safety, efficacy and electrophysiological parameters of LBBP in octogenarian (≥80 years) population showed that LBBP was successful in 10 out of 11 patients with Mean age 82.1 ± 2.5 yrs. Follow up duration 7.7 months(range4–10). With Indication for pacing included atrioventricular (AV) block 5 patients, Left bundle branch block (LBBB) with low ejection fraction in 4 patients, sinus node dysfunction in 1. QRS duration reduced from 145.9 ± 27.7ms to 107.1 ± 9.5ms (*p* value <0.00001) LV ejection fraction increased from 47.6% to 58.4% after LBBP (*p* value0.017). Pacing threshold was 0.58 ± 0.22 V and sensed R wave 17.35 ± 6.5 mV and it remained stable during follow up.

LBBB with low EF patients also showed similar reduction in QRS duration along with improvement in LVEF.

Strocchi M et al [31] conducted study compare changes in ventricular activation induced by HBP, LBP, left ventricular (LV) septal pacing, BiV-endo, and biventricular epicardial (BiV-epi) pacing which showed HBP was superior to BiV-endo and BiV-epi in terms of reduction in LV ATs and interventricular dyssynchrony ($P < .05$). LBP reduced LV ATs but not interventricular dyssynchrony compared to BiV-epi and BiV-endo pacing. RV latest AT was higher with LBP than with HBP (141.3 ± 10.0 ms vs 111.8 ± 10.4 ms). Optimizing AV delay during LBP reduced RV latest AT (104.7 ± 8.7 ms) and led to comparable response to HBP. In case of complete AV block, BiV-endo septal pacing was equivalent to LBP.

6.3 AIMS AND OBJECTIVES OF THE STUDY

1. To study safety, success rate, complications and effects of physiological pacing and its short-term clinical outcomes on 6 months of follow up in patients requiring pacing for bradycardia indications.
2. To study and compare Electrocardiogram and Transthoracic Echocardiographic parameters of Physiological pacing post pacemaker implantation and on 6 months of follow up.
3. To Study and compare lead parameters of Physiological pacing, post-pacemaker implantation and on 6 months of follow up.

7.0 MATERIALS AND METHODS

7.1 SOURCE OF DATA

The study population will consist of consecutive patients meeting inclusion criteria for pacemaker implantation with an initial attempt to perform Physiological pacing technique following informed consent from 1st August 2021- 30th July 2022 with follow-up of 6 months till 31st January 2023 at Dayanand Medical College & Hospital.

7.2 METHOD OF COLLECTION OF DATA

INCLUSION CRITERIA:

1. Patients with Sinus node dysfunction, Atrio-ventricular blocks, Left Bundle Branch Block, Bi-Fascicular blocks with Class I and IIa Recommendation for pacemaker implantation as treatment of choice according to 2018 ACC/AHA/HRS Guideline on the Evaluation and Management of Patients with Bradycardia and Cardiac Conduction Delay. [32]

EXCLUSION CRITERIA:

1. Lack of Informed consent
2. Patients with Sinus node dysfunction, Atrio-ventricular blocks, Left Bundle Branch Block and Class IIb, III recommendation according to 2018 ACC/AHA/HRS Guideline on the Evaluation and Management of Patients with Bradycardia and Cardiac Conduction Delay.[32]
2. Presence of septal scar on Transthoracic echocardiographic assessment.
3. Uncertainty of indication due to probable reversible cause of bradycardia.
4. Patients with current or recent history of severe, progressive, or uncontrolled renal, hepatic, hematological, gastrointestinal, metabolic, endocrine, pulmonary, cardiac, neurological disease.

STUDY DESIGN: A Retro-Prospective study will be conducted at Dayanand Medical College and Hospital, Ludhiana, from August 1, 2021 to 30th July 2022 with follow-up of 6 months till January 31st , 2023.

METHODOLOGY: Patients meeting inclusion criteria will be analyzed at baseline for NYHA functional class, Electrocardiogram, QRS duration, QRS axis, QRS transition zone, Chest X-ray and transthoracic echocardiographic parameters. Following which Patients will undergo an attempt for Physiological pacing as an initial method of pacing. Post Procedure Electrocardiogram for Paced QRS [ms], QRS axis, QRS transition zone, LVAT, Echocardiograph and lead parameters will be measured and any complications will be noted. These patients will be followed up after 6 months for reassessment for NYHA functional class, Electrocardiogram, lead parameters, transthoracic echocardiographic parameters and any complications or requirement for lead revision. At end of study Implant success rates will be measured along with comparisons of between baseline, post-implantation and 6 months and data collected will be statistically analyzed using appropriate methods.

OUTCOME: It is hypothesized that His and Left bundle branch pacing will be easier to perform with a high successful rate of implantation, Threshold V @ 0.5ms will be in range of 0.5 to 0.8mv ,[17] QRS durations will be narrower following procedure with a range of 111-136 ms,[17] with non-significant difference on follow-ups, R wave amplitude will be in range of 9.1 mv-11.99 mv[17]. Physiological pacing can improve clinical profile decrease in functional class and improve echocardiographic parameters with an increase in ejection fraction.

STATISTICAL ANALYSIS: Data will be described in terms of range; mean ±standard deviation (± SD), frequencies (number of cases) and relative frequencies (percentages) as appropriate. Comparison of quantitative variables between the study groups will be done using Student t-test and Mann Whitney U test for independent samples for parametric and non-parametric data respectively. Comparison of quantitative variables within the study groups will be done using paired t-test and Wilcoxon rank sum test for independent samples for parametric and non-parametric data respectively. For comparing categorical data, Chi square ($\chi 2$) test will be performed and exact test was used when the expected frequency is less than 5. A probability

value (p value)less than 0.05 will be considered statistically significant. All statistical calculations will be done using (Statistical Package for the Social Science) SPSS 21version (SPSS Inc., Chicago, IL, USA) statistical program for Microsoft Windows.

7.3 DOES THE STUDY REQUIRE ANY INVESTIGATIONS OR INTERVENTIONS TO BE CONDUCTED ON PATIENTS OR OTHER HUMANS OR ANIMALS? IF SO, PLEASE DESCRIBE BRIEFLY.

NO

7.4 HAS ETHICAL CLEARANCE BEEN OBTAINED FROM YOUR INSTITUTION IN CASE OF 7.3?

ATTACHED HEREWITH

8.0 LIST OF REFERENCES

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PROFORMA

Enrolment date: ---------- Sr. No. ----------

Name: ---------- Age: ----------

Adm No/ MRD No. : ----------/---------- Address: ----------

Occupation: ---------- Phone no. ----------

HISTORY:

NYHA CLASS- Baseline- ; 6 months-

Physical Examination:

Height: ---------- BSA: ----------

Weight: ---------- BMI: ----------

Systolic BP: ---------- Diastolic BP: ----------

Pallor: ------ Icterus: ---------- Cyanosis: -------- Edema: ---------

JVP: -------- Ascites: ---------- LAP: ----------

Signature of Candidate Signature of Supervisor

CVS Examination: ----------

	Positive findings	
Inspection		
Palpation		
Auscultation	Aortic area	Pulmonary area
	Mitral area	Tricuspid area

Past H/o

Diabetes Mellitus	
Hypertension	
Arrhythmia	
CAD	
COPD	
Valvular Heart Disease	
Cardiomyopathy	
Congestive heart failure	

Diagnosis-

Indication for Pacemaker-

COR(ACC/AHA)-

Investigation:

Signature of Candidate

Signature of Supervisor

Chest X-Ray Finding -

ECG Findings

	BASELINE	Post- Procedure	6MONTHS
Rate			
Rhythm			
QRSd			
QRS axis			
QRS transition zone			
R wave Amplitude in V1			
LVAT			

2D ECHOCARDIOGRAPHY

	Baseline	Post-Procedure	6Months
LA Size (mm)			
Aortic root (mm)			
Right Atrium (mm)			
LVID(S)			
LVID(D)			
RVID(D)			
IVST (s)			
IVST (d)			
LVPW (s)			

Signature of Candidate

Signature of Supervisor

LVPW (d)			
Ejection fraction (%)			
MR (mild/mod/severe)			
E/A			
AR (mild/mod/severe)			
TR (mild/mod/severe)			
PR (mild/mod/severe)			
Pericardial effusion			
SPWMD (M Mode)			
SPWMD (TDI)			
IVMD			
LVDV			
LVSV			

Lead Parameters

	Post Procedure	6months
Pacing Threshold		
Impedance		
Amplitude		

Complications-

Signature of Candidate

Signature of Supervisor

INFORMED PATIENT CONSENT

Date: _____

I.....D/o, W/o, S/o.....
.....am willing to participate in the study **"A RETRO-PROSPECTIVE STUDY OF PHYSIOLOGICAL PACING AND ITS SHORT TERM OUTCOMES."** The procedure with its complications has been explained to me in local vernacular language. I have fully understood that no special tests and extra expenditure in any form, merely for the purpose of thesis is being carried out. I am free to opt out the study any time without assigning any reason.

.....
Signature of the Witness

Name:

.....
Signature of the patient

Signature of Candidate

Signature of Supervisor

मरीज अनुमति फार्म

तिथि _____

मैं _____ पत्नी/पुत्र/पुत्री _____

निवासी _____

इस शोधकार्य **"A RETRO-PROSPECTIVE STUDY OF PHYSIOLOGICAL PACING AND ITS SHORT TERM OUTCOMES."** में भाग लेने के लिए सहमत हूँ। मैं इस शोधकार्य में भाग लेने के लिए अपनी स्वेच्छा से तैयार हूँ। मैं पुष्टि करता/करती हूँ की यह स्वीकृति देने के लिए मुझे कोई आर्थिक प्रलोभन नहीं दिया गया और न ही दबाव डाला गया है। मुझे इस शोधकार्य का उद्देश्य स्पष्ट कर दिया गया है और मुझे यह विश्वास है की यह विज्ञान और मानवता के लाभ के लिए है। मुझे इस शोधकार्य में होने वाले जोखिम के बारे में समझा दिया गया है और मेरी समझ में यह जोखिम बहुत मामुली है।

मैं इस शोधकार्य में भाग लेने के सम्बन्ध में किसी भी समय अपनी अस्वीकृति व्यक्त कर सकता/सकती हूँ और मेरे अस्वीकृति व्यक्त करने का मेरे इलाज पर कोई प्रभाव नहीं पड़ेगा।

_____

गवाह के हस्ताक्षर

नाम:

_____

रोगी के हस्ताक्षर/अंगूठे का निशान

नाम:

_____

अन्वेषक के हस्ताक्षर

_____

विद्यार्थी के हस्ताक्षर

ਮਰੀਜ਼ ਰਜ਼ਾਮੰਦੀ ਫਾਰਮ

ਮਿਤੀ_____

ਮੈ_____ਪਤਨੀ/ਪੁੱਤਰ/ਪੁੱਤਰੀ_____

ਵਾਸੀ _____

"A RETRO-PROSPECTIVE STUDY OF PHYSIOLOGICAL PACING AND ITS SHORT TERM OUTCOMES." ਤੇ ਚਲ ਰਹੀ ਖੋਜ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਰਜ਼ਾਮੰਦ ਹਾਂ। ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਮੈ ਆਪਣੀ ਮਰਜ਼ੀ ਨਾਲ ਤਿਆਰ ਹਾਂ। ਮੈ ਇਹ ਦਸਣਾ ਚਾਹੁੰਦਾ ਹਾਂ/ ਚਾਹੁੰਦੀ ਹਾਂ ਕੇ ਇਹ ਰਜ਼ਾਮੰਦੀ ਦੇਣ ਵਾਸਤੇ ਮੈਨੂ ਕਿਸੇ ਵੀ ਤਰਾਂ ਦਾ ਲੋਭ-ਲਾਲਚ ਨਹੀ ਦਿੱਤਾ ਗਿਆ ਅਤੇ ਨਾ ਹੀ ਕੋਈ ਦਬਾ ਪਾਇਆ ਗਿਆ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਦਾ ਮਨੋਰਥ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਭਰੋਸਾ ਦਵਾਇਆ ਗਿਆ ਹੈ ਕੇ ਇਹ ਖੋਜ ਵਿਗਿਆਨ ਅਤੇ ਮਾਨਵਤਾ ਦੀ ਭਲਾਈ ਲਈ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਵਿਚ ਹੋਣ ਵਾਲੇ ਖਤਰੇ ਬਾਰੇ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਯਕੀਨ ਹੈ ਕੇ ਇਹ ਖਤਰਾ ਬਹੁਤ ਮਾਮੂਲੀ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਦਾ ਢੰਗ – ਤਰੀਕਾ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ।

ਮੈ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਬਾਰੇ ਆਪਣੀ ਰਜ਼ਾਮੰਦੀ ਕਿਸੇ ਵੀ ਸਮੇ ਵਾਪਸ ਲੈ ਸਕਦਾ ਹਾਂ/ ਸਕਦੀ ਹਾਂ ਅਤੇ ਮੇਰੀ ਰਜ਼ਾਮੰਦੀ ਵਾਪਸ ਲੈਣ ਦਾ ਮੇਰੇ ਇਲਾਜ ਤੇ ਕੋਈ ਅਸਰ ਨਹੀ ਹੋਵੇਗਾ।

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ਗਵਾਹ ਦੇ ਹਸਤਾਖਰ

ਮਿਤੀ_____

ਪਤਾ _____

_____
ਮਰੀਜ਼ ਦੇ ਹਸਤਾਖਰ

ਮਿਤੀ_____

ਪਤਾ _____

_____
ਨਿਰੀਖਕ ਦੇ ਹਸਤਾਖਰ

_____
ਸਿਖਿਆਰਥੀ ਦੇ ਹਸਤਾਖਰ